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THE SURGERY OF CANCER*

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LET us stand back for a moment and inspect the edifice of knowledge already erected on the surgery of cancer. This paper considers the history of the basic concepts involved in the modern surgery of tumors and attempts to demonstrate the inter-relation in the growth of these ideas; this perspective will permit a prognosis to be uttered for the surgical discipline in cancer. Obviously all three efforts must be brief and sketchy; a list of all the contributors to cancer surgery would read like the catalogue of the ships in the second book of the Iliad or the begat series in Genesis.

I suppose that a defense of the historical approach is never necessary. Although its methods are occasionally tiresome to nonprofessional historians, history is often of interest, and it becomes important if one can see in past performance a clue for future advance.

It might well be asked why the surgery of cancer should be discussed at a celebration of the introduction of anesthesia. There are several reasons — the development of the modern concepts of neoplastic disease was coeval with and largely consequent on the development of modern surgery. Clearly, before pain had been controlled and the relaxation of muscles had been secured, surgical operations on internal organs were possible to such a limited extent as to be practically negligible. Certainly, the surgery of tumors of the viscera comprises a large percentage of the surgical task and the opening of this field awaited anesthesia for its development. Also, the famous operation that introduced the use of ether in surgery was performed by Dr. Warren on a vascular tumor of the neck.

A century ago cancer was emerging from a period of empiricism and superstition in which the disease had been completely shrouded in mystery. Some attempts at description of tumors had been made, but medicine was in the Paleozoic age, innocent of laboratories and nearly devoid of the correlation of the clinical state with dead-house findings, despite Morgagni's *De Sedibus*.[1] Before 1846 few studies of cells or tissues had been made, and cellular pathology was unknown. At that time, in his second published paper entitled "Weisses Blut," Virchow had just attributed correctly the pale character of the blood in leukemia to an excess of white corpuscles.

As representative of early American surgical thought about neoplasms I cite the experience of Warren,[2] who in 1839 described the status of cancer surgery at the Massachusetts General Hospital just before the discovery of anesthesia. He stated that an "exact discrimination between different kinds of tumors is very important to the practitioner of surgery." He added: "The opinion he may offer in such cases will soon be put to a severe and publick test; for the course of these diseases lies open to the view of the patient and his friends and the result must be known to them." At that time, however, so little was known about disease that diagnosis was often impossible. The differentiation, for example, between granulomas and neoplasm was difficult, although scrofulous lesions were well recognized. Cancer, according to Warren, was not regarded as a specific disease: "It has a variety of forms, of causes and of habitudes of action. There is nothing specific in it unless you call its incurable disposition specific." A constitutional predisposition to cancer was recognized, and the disease was thought to occur frequently after violence. Tobacco was recognized as a factor in lesions of the mouth and lower lip.

Two species of cancer were regarded as separate entities easily distinguishable from each other — namely, carcinoma and fungoides. Carcinoma, or scirrhus, was characterized by its hardness and its tendency to ulceration. The term "fungoides" (sarcoma) was used for tumors that were soft and had a tendency to bleed easily.

In cancer of the breast Dr. Warren recognized that "enlargement of the glands in the axilla commonly took place from the extensions of the diseased action along the absorbent vessels," and that

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when the lymph nodes were enlarged the disease was usually incurable. Thyroid tumors were believed to be a disease of inland countries and of territories situated on the banks of rivers, and the recommended treatment was the internal use of burnt sponge and of iodine. Tumors were frequently of tremendous size before operation was undertaken, often weighing ten to twenty pounds.

The surgical treatment, which was largely superficial, was confined to tumors of the head, except for the cranial contents, and the neck, breast, extremities and skin. Strong men had important roles in the operation as technical assistants. Extensive operations on the jaws were often undertaken. The surgical procedures were threefold, consisting of excision, mass ligature with stout cords transfixing the tumors at right angles by the aid of needles either straight or crooked or the actual cautery. In procedures of excision skin flaps were raised when possible and resutured loosely at the end of the operation. Bleeding and air embolism often provided a serious difficulty.

The modern reader is impressed by three characteristics of preanesthetic surgery: the deficiency of pathological knowledge at that time, the often reckless celerity of the surgical procedure and its attendant agonies. The surgeons of a hundred years ago were men of intelligence whose mental powers we can, with charity, rate equal to our own. Was everything that they did inferior to the practices of today? Obviously not; one gains the opinion that in anatomic knowledge, at least, the surgeon was rather better informed than the average surgeon today, since anatomic dissection was nearly the only investigative outlet for diligent and thoughtful surgeons.

The necessity for rapid operations required that the procedure be well thought out. The following advice of Warren is still apposite to surgical practice:

> An operator should not be satisfied with tracing a plan in his mind only. It should be fairly written out; and he should imagine all possible difficulties and embarrassments and put them in writing.

The evolution of the surgery of cancer from this elementary position was biphasic and rested on the development of some working concepts of the disease, as well as on the establishment of better surgical ideas. Both aspects had to be developed simultaneously, since both required much the same methods — the methods of science. Progress in medicine has always been dependent on the advances of pure science to a peculiar extent. A secondary or reading knowledge of science has usually provided an insufficient stimulus for the discovery or application of scientific knowledge to the clinical problems. Working with phenomena gives a vastly more intimate familiarity with the effects of nature than books do, and for this reason the greatest advances in medicine have been made by active participants in research. Also, the scientific indoctrination of close observation and precise thought has provided a fresher attitude to the puzzles of medicine than was possible with bedside study alone. These are concepts of primary importance because they provide historical justification for the necessity of surgical laboratories and research workers in the clinical departments.

The history of cancer surgery also emphasizes the influence of the schools of surgery, which have always formed around energetic and intelligent leaders; this fact is reiterated below. There are two obvious reasons why the momentum of a great surgical school forms a self-catalyzing cycle: a successful department is apt to attract the brilliant students, who in turn contribute to the success of the clinic. Thus, the school of pathology founded by Johannes Müller in Berlin in addition to the founder had two members who made large contributions to the knowledge of tumors.

The concept of organization of the body in cellular units depended on the development of the achromatic microscope by Silligues, of Paris, in 1824; Müller[3] himself soon undertook the microscopical study of cancer cells (his findings were published in 1838), but the morphologic studies of that time were at a primitive level. In 1852 one of his students, Adolf Hannover,[4] of Copenhagen, set cancer of the skin apart from other cancers because of its low rate of growth and coined the name "epithelioma" for this group of neoplasms, which he regarded as more benign than the tumors of the viscera. Another of the contributions of Hannover was the advocacy of biopsy of superficial lesions to establish a pathological diagnosis. Rudolf Virchow,[5, 6] who graduated from the University of Berlin in 1843, was another of Müller's pupils who exerted a great influence on pathology — indeed, he was one of the fathers of this discipline. Virchow's great contribution was the recognition of the importance of the cell in pathologic processes. Before Virchow the cellular structure of cancerous tissue had been recognized, but the cells had been thought to be subsidiary to an underlying humoral "blastema," which was regarded as a sort of primary fluid from which all structures arose. Haagensen[7] estimates Virchow's discovery as follows: "With his dictum 'Omnis cellula e cellula' Virchow swept away this erroneous conception and firmly established the cell as the fundamental unit in which disease processes operate."* This law, which stated that all living cells represented an uninterrupted continuum, has had functional value in the elucidation of disease. No one has been able to disprove it, and it has been largely unquestioned recently, although it is probably wrong. Perhaps, in some of the back waters and bayous of the world molecular conjunctions are occurring to effect reproducibility or life.

*Haagensen[7] has compiled an interesting bibliography of some of the source material concerning the early history of the development of the pathology of cancer.

The term "sarcoma" had been used by Galen in a restricted sense in describing abnormal fleshy growths in the nares, and as already mentioned, this word had been adopted by surgeons in the sense of any soft and highly vascularized growths. The modern definition of sarcoma was laid down by Virchow[6] as an abnormal growth belonging to the general group of the connective tissues. Virchow, however, erroneously believed that all malignant tumors arose from connective tissue.

The definition of carcinoma as an atypical epithelial growth of either surface or internal lining cells was not agreed on until the work of Thiersch[8] and Waldeyer.[9] In 1865 Carl Thiersch, of Erlangen, studied skin carcinoma by means of free hand sections made with a razor, staining the slices with ammoniated carmine. He was able to establish the topographic continuity of deep-seated masses of subcutaneous malignant epithelial cells with the surface layer and concluded that they arose from the epithelium rather than from connective tissue. He also showed that in this condition the presence in the lymph nodes of nests of cancer cells was due to the metastasis of the cells of the skin carcinoma. The proof ably developed by Thiersch of the epithelial origin of cutaneous carcinoma was confirmed in Breslau by Waldeyer, who in 1872 extended the idea to show that adenocarcinoma arose from epithelium in all other parts of the body; the evidence was simple and consisted of the demonstration of the physical continuity between the normal epithelium and the carcinoma.

Advances in the general field of surgery made possible the surgical treatment of external cancers, but the development of surgical technics for the treatment of internal cancer required the discovery and application of the principles of surgery. The formulation of the principles of surgery made tremendous strides in the last century and is still going on. These principles are probably not yet definitive or insusceptible of clarification, and consequently they cannot be regarded as a finished product incapable of improvement.

The great principles of surgery are perhaps six in number: control of pain; a deliberate operative procedure undertaken without haste; adequate exposure of the lesion; control of bacteria; maintenance of the optimum physiologic state; and accurate preoperative diagnosis.

Three of these principles were made possible by the introduction of ether anesthesia, which is no doubt the greatest single contribution in the development of surgery. The abolition of pain not only was a humane measure of significance but also made possible an unhurried and thoughtful operation with adequate exposure of the lesion. No longer was it necessary to make a reckless attack to correct an abnormal process in which haste often led to complicating accident.

Control of bacteria next received attention, since a brilliant operative maneuver frequently became undone in the postoperative period. The control of bacteria in the external environment, being simpler, was developed first and in the last century, whereas chemotherapy against the internal bacterial pathogens has been introduced only recently. The concepts and experiments of Lister[10, 11] remain among the simplest and most productive products of the surgical mind. The Listerian ideas and the use of phenol, together with the milder antiseptic agents that were developed later, remain important. The killing of bacteria by sublimate and heat sterilization led to the introduction of the aseptic technic by von Bergmann,[12] and this was a significant practical addition to antisepsis. Some partial control of internal bacteria through chemotherapy has been achieved only in the last fifteen years, dating from the introduction of prontosil in 1932 by Domagk[13]; this discovery, of course, was greatly improved with the later elucidation of its prosthetic group, the sulfonamide nucleus, and its mode of action by way of competition with para-amino benzoic acid. The use of natural antibiotic products elaborated by soil bacteria and molds with their partial purification through the work of Dubos and his luckier contemporaries, Fleming, Waksman and others, has profoundly affected surgical practice.

The maintenance of the optimum physiologic state did not arise as a full-blown concept until the last decade. Since ether had rendered possible extensive operations, the necessity to prevent exsanguination became apparent, and the control of bleeding was obtained by many ingenious technical advances. An important technical detail was the application of the lock device to hemostatic forceps by Spencer Wells and the French school (Pean); this was of practical value since it made possible such movements as that of the Halsted[14] school, which introduced meticulous and immediate hemostasis. The recognition of the blood groups of man by Landsteiner[15] (1901) and the development of blood transfusion and the blood substitutes, such as plasma and other substances, saved many lives. After many years it developed that hemostasis and blood transfusion were not enough; the general nutritional state of the organism regarding fluid, electrolytes, vitamins and carbohydrates has importance as well. Within recent years, largely as a result of the work of Cannon and his associates[16] in Chicago, it has been appreciated that the body proteins are of particular significance since states of protein deficiency are associated with a deficient antibody pool in the organism and consequently with deficient natural defences; obviously, the protein status of the surgical patient cannot be disregarded or the treatment of protein deficiency neglected. Just as Virchow recognized that the basis of pathology was the tissues and their cells, the surgeon must realize that a surgical procedure is done on

protoplasm and that the chemical reactions and functions of this jelly of the cells are of considerable significance to him.

Of particular importance in cancer surgery is the recognition of a neoplasm through accurate diagnosis and in an early stage of the life of the tumor. Clearly, the surgery of advanced tumors is a pessimistic performance. The diagnosis awaited physical and chemical means for its development. The physical instruments of greatest value were the electric lamp of Edison and the x-rays of Roentgen[17] (1895). The application of tiny electric lamps to the cystoscope by Nitze[18] in 1887 made endoscopic cystoscopy possible and led to the development of urology as a specialty. The discovery influenced medicine considerably, and Nitze acknowledged in his first paper that the diagnosis of bladder tumors was the great triumph of his method. Menlo Park also made possible direct examination of the rectum, sigmoid, stomach esophagus, bronchi and other previously inaccessible regions. The impact of Roentgen's discovery on diagnosis was so large as to be incalculable and its use revolutionized the detection of disease in every field of medicine.

Chemistry has also contributed to the diagnosis of surgical disease, especially in cancer. Indirect methods concern concentration of radio-opaque dyes in the gall bladder and urinary tract as introduced by Graham and Cole[19] (1924) and Binz[20] (1930) respectively. Direct methods of chemical diagnosis of cancer are concerned with the urinary excretion of proteins derived from cancer cells, such as the albumose of Bence-Jones[21] (1848) in multiple myeloma, of melanin in melanosarcoma and of chorionic gonadotropin in testicular tumor as discovered by Zondek[22] in 1930. In prostatic cancer tumor products are also detectable in the blood in the form of certain enzymes, as demonstrated by Gutman and Gutman[23] in 1938. Since the aim of diagnosis is to recognize disease without seeing the patient, it is clear that the laboratory must assume large importance as the science develops.

The surgical problems of cancer were largely brought into focus and the principles of surgical treatment developed in the evolution of the handling of patients with cancer of the female breast. This was natural for several reasons, especially because mammary cancer is frequent. Contributory also were the facts that the primary lesion and the lymph nodes draining the breast were superficial and easy to examine and that the surgical treatment did not involve violation of a body cavity. In 1867 Moore,[24] of London, was one of the first surgeons to appreciate that the recurrence of a breast cancer was due to incomplete removal of the tumor; it had previously been thought that these lesions represented an entirely new neoplasm developing on an organic or constitutional basis. Moore proposed that when the adjoining skin or axillary lymph nodes are involved by cancer they should be removed in one mass, since it is desirable to avoid cutting into the tumor or even exposing it at operation.

The value of this concept of block dissection was confirmed and the technic widened by Volkmann, who discovered that cancer cells frequently infiltrated the fascia covering the pectoralis major muscle so that this fascia was routinely removed by him; Halsted[14] (1890) showed that technically the best way to do this was to remove the pectoralis muscles, and he also advocated the removal of large amounts of skin surrounding the tumor. Each technic resulted in a larger percentage of cures than previously, and axillary dissection became a routine whether or not the lymph nodes were suspected of being grossly involved by the tumor.

The surgery of visceral cancer was developed in a definite time sequence — namely, abdominal and genitourinary tracts, central nervous system and lastly the chest.

Visceral surgery could not be developed before anesthesia or antisepsis, but with these aids the essential methods were rapidly introduced. The principal methodology of abdominal surgery was devised largely in the Billroth school in Vienna. Theodor Billroth was a magnetic leader and a tireless and intelligent worker as well as a *bon vivant*. His school worked out many of the technics of stomach and bowel resection on animals in the surgical laboratory, and this approach in itself was a contribution to surgical investigation of first-class importance. In 1881 Billroth[25] made the first resection of the pylorus for gastric cancer and performed many intestinal resections between 1878 and 1883. A Billroth pupil, Anton Wölfler,[26] devised the technic of gastroenterostomy in 1881, and another student, Mikulicz[27] (1903) introduced obstructive resection with exteriorization of the large bowel for carcinoma; both procedures advanced cancer surgery. Surgeons throughout the world soon added many technical refinements to abdominal surgical technic.

Tumors of the urinary tract were seldom treated before the advent of precise diagnostic methods. The first tumor of the bladder to be removed by *sectio alta* was operated on by Billroth[28] in 1874, the diagnosis having been made by urethrotomy with digital palpation of the neoplasm in the vesical cavity. Cystoscopy, ureteral catheterization and pyelography converted a *terra incognita* into a field characterized by diagnostic precision. Although the electrically lighted cystoscope of Nitze had made possible the diagnosis of bladder tumors, Nitze had unsuccessfully tried to catheterize the ureters, since he had no way of manipulating the tip of the catheter. A remarkably interesting Cuban, Joachim Albarran,[29] professor of urology in Paris, solved the problem by devising a cystoscope with a movable arm to provide leverage and thus to guide the catheter into the ureteral ostium. Ureteral catheterization and the subsequent introduction of contrast

radiography by Voelcker and von Lichtenberg[30] (1905) were real steps forward in the diagnosis of renal neoplasms. The perineal approach to the prostate and total prostatectomy introduced by Young[31] (1906) made possible the excision of early cancer of the prostate gland. The introduction of high-frequency currents and their application to cystoscopic fulguration by Beer[32] have added much to the treatment of vesical neoplasms.

The surgery of tumors of the nervous system was developed chiefly because of the efforts of the Queen Square group in London and of Cushing[33] and Dandy[34, 35] in the United States. In 1885 Bennett and Godlee[36] first localized and removed a brain tumor, although unfortunately the wound in this case became infected and the patient died a month later of meningitis. Gowers and Horsley,[37] in 1888, first localized and extirpated a tumor of the spinal cord, the patient making a complete recovery.[38] The contributions of Cushing[33] in the field of tumors of the nervous system were manifold; perhaps his most significant contributions were the development of a refined deliberate surgical technic, new approaches for the cerebellar tumors and a classification of neoplasms of the brain. The Cushing methods transformed what was previously a highly dangerous operative attack into a comparatively safe one. The fertile mind of another Hopkins product, Walter Dandy,[34, 35] contributed the diagnostic tools of encephalography and ventriculography and devised many clever procedures — for example, a new surgical approach for the treatment of tumors of the acoustic nerve.

The development of the surgery of intrathoracic neoplasms was delayed until methods were found to prevent pulmonary collapse. The solutions offered for the problem became progressively simpler. In the research laboratory of an industrial concern today there is a sign that reads as follows: "When the solution of your problem is known, it will be found to be simple." Methods of preventing collapse of the lung, such as the differential pressure cabinets of Sauerbruch,[39] were cumbersome and difficult to use and were soon replaced by intratracheal insufflation; the present methods of dispensing anesthetic gases from tanks under pressure allow the lung to be kept at any required degree of expansion or collapse by the use of a simple facial mask.

Partial pneumonectomy for tumors of the lung was accomplished by Sauerbruch[39] in 1926 and by Churchill[40] in 1933 with good results, and the entire lung was first removed for cancer by Graham and Singer[41] in 1933. In the early cases fear of the huge empty pleural cavity was present, and the space was obliterated by thoracoplasty; this was a groundless fear, however, and Rienhoff[42] (1933) showed that the cavity became obliterated by compensatory pulmonary expansion, so that plastic operations on the chest wall were dispensable.

The surgical treatment of tumors of the thoracic esophagus was late in development. In 1913 the first successful esophagectomy was carried out in New York by Torek,[43] who resected the esophagus, bringing the proximal portion externally through a cervical incision and feeding the patient by gastrostomy. This technical procedure was superseded by the work of the Japanese surgeon Ohsawa,[44] who in 1934 performed successful transthoracic resection of the neoplasms of the esophagus and of the cardia of the stomach with esophagojejunostomy. This procedure has been refined and made less dangerous by the work of many thoracic surgeons, especially in America.

In orthopedic surgery the development of basic principles has influenced the surgery of bone sarcoma. Codman recognized the fact that giant-cell tumors of bone were benign lesions that did not require amputation of the limb. In 1938 Phemister[45] discovered that malignant bone sarcomas could often be cured by local resection of the involved part with preservation of the extremity through bone grafting. This is in accord with the ideas of modern cancer surgery — that is, there is no need to cut off the head to cure a brain tumor.

In the nineteenth century surgeons were concerned with descriptive pathology, with concepts of the grosser aspects of cancer and with the evolution of some of the simpler principles of surgery. With the close of this period the gross description of tumors had been rather well made, and the era of laboratory experimentation was fairly begun. Until disease can be reproduced in the laboratory, advances other than the descriptive ones — and description is necessarily limited in scope — must be uncertain and irregular. In the present century the chief achievements have been in the experimental production of tumors, in their treatment with radiant energy and in the beginning of chemotherapy. Owing to refinements in technic, tumors of nearly all the viscera have become surgically accessible. Evidently, most of the major technical obstacles of the anatomy and physiology involved in the approach to cancer in whatever locus have been solved.

In the research laboratories remarkable strides have been made since 1900. Transplantable tumors have become available since the work of Jensen[46] in 1903, and a wide variety of tumors of chickens, rabbits, rodents and frogs have been discovered. The viruses have been seriously implicated in certain neoplasms, as first shown by Rous[47] in 1911. The production of cancer in the laboratory with pure chemicals has been achieved.[48] The endocrine basis and methods for the experimental production of breast cancer have been discovered.

The diagnosis of tumors by chemical means was mentioned above. This is the newest and a promising field in cancer research, and it is striving to fill a grave hiatus. The importance of chemical investigation of the activity of tumors is that they

provide a measure. The greatest handicap to research on cancer is the lack of a yardstick — something that can be measured at daily intervals. This can be done only for tumors of the blood-forming organs, for osteogenic sarcoma and for cancer of the prostate.

Another of the recent developments in cancer is the chemical treatment of neoplasms of epithelial and hemopoietic tissues. Some progress has been made in the chemotherapy of prostatic and breast cancer, in which improvement has been profound and prolonged in many cases. Remissions of advanced neoplasms are being produced by chemotherapy. Although the treatment of carcinoma by medicines has been exceedingly limited, enough progress has been made so that it may be predicted with confidence that the medical therapy of cancer will increase in the future.

Therefore, I can now approach the somewhat delicate question of the prognosis of the surgery of cancer, realizing that prognosis and prophecy bear a close relation. The technical accomplishments of the surgeons have been brilliant and splendid but only when the lesion is essentially localized. The inherent defect in the surgical method is the impossibility of removal of widespread neoplasms, and the prognosis for treatment by classic surgery in metastatic cancer is poor. Nothing, however, stands in the way of surgical research on neoplasia, and much information may be expected from the surgical laboratories.

The constantly expanding significance, for the advance of medicine, of the research laboratory conducted in connection with a surgical clinic has been repeatedly emphasized. Since the surgical departments at present have greatest access to and often the greatest interest in the clinical course of patients with cancer, it is essential that the surgical laboratory take the lead in converting the surgery of cancer into medical treatment — this self-effacement being in keeping with the great tradition of surgery.

Fortunately, the avenues of research provide unlimited scope for constructive thought, and the technics of surgery applied to research problems in cancer may be developed to a high state of intellectual polish. At the risk of sounding hortatory, I wish to say that it devolves on the surgeons to make more investigation of tumors in their broader aspects. The researches are not without interest, and the opportunity to contribute to medicine through participation in investigations on cancer is large; hence, the prognosis for the broad surgical discipline in cancer is excellent.

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OBSERVATIONS ON A FAMILY EPIDEMIC OF INFECTIOUS HEPATITIS*

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AN epidemic of infectious hepatitis occurring in 9 of 10 children in a single family was followed for five months in New York City. Such a high incidence of the disease in a group is unique in itself; in addition, these cases offered special information on four separate aspects of the disease — namely, epidemiology, the comparative value of certain liver-function tests, the occurrence of spider angiomas in the acute stage of infectious hepatitis and the incidence of subicteric cases.

All members of the family were observed in the Outpatient Department of the Rockefeller Hospital, where liver-function tests were performed at regular intervals; 3 were admitted to the hospital for special studies. Friends of the family who came in contact with the children were also observed; 2 of this group were hospitalized with infectious hepatitis. The chief source of information regarding the illness of the children was the mother of the family, a trained nurse familiar with liver disease.

Several descriptions of family epidemics of infectious hepatitis have appeared in the literature in recent years.[1-4] The mode of spread in these families was generally believed to be droplet infection. Recent work on human volunteers has shown that the disease can be transmitted experimentally to man by parenteral injection of small amounts of infective serum, by ingestion of infective serum or feces and by the spraying of infective feces into the nasopharyngeal passages.[5-7]

During an epidemic in a summer camp, Neefe and Stokes[8] found the virus of infectious hepatitis in the drinking water. This work, together with that of others[9, 10] indicates that contaminated water may be the source of infection in certain epidemics. Milk and food have also been implicated in a few outbreaks.[11, 12] A characteristic of epidemics begun by contaminated food or water is their explosive nature, although sporadic cases often followed. Most of the epidemics described in the literature, however, are characterized by the serial occurrence of cases over a period of several months with a history of contact between the majority of patients. Sometimes, the contact appeared to be slight, and this led to postulation of droplet and air-borne infection. In view of the recent comparatively easy transmission of the disease in human volunteers by infective fecal material, spread by contact now seems more probable. The family epidemic under consideration in this paper offers certain information on this subject.

Brief summaries of the case records are as follows:

CASE 1. On November 13, 1945, this 10-year-old girl developed nausea, vomiting, abdominal pain and fever. These symptoms persisted for 2 days and were followed by a period of anorexia that lasted for 1 week. Considerable fatigue was noted, and the patient was forced to stay out of school for 10 days. Recovery was rapid, and except for a weight loss of 7 pounds, the patient felt fine by November 20. No jaundice was noticed.

Physical examination on January 26 disclosed a definite spider angioma over the left shoulder that blanched well on pressure. The liver and spleen were not palpable or tender. Liver-function tests revealed no abnormalities. On March 26 there were no changes except that the spider angioma had decreased in size and no longer blanched on pressure. On August 8 the angioma had completely disappeared.

CASE 2. On November 19, 1945, this 8-year-old boy developed pain in the upper abdomen and a loss of appetite that persisted for 2 days. A definite tenderness in the upper right side of the abdomen was noted by his mother. He stayed out of school for 1 day. Several nosebleeds occurred at that time — these were the first that had ever been noted. Recovery was rapid, and there were no further complaints. No jaundice was noticed.

Liver-function tests on January 25 disclosed no abnormalities.

Physical examination on January 26 revealed that the liver and spleen were not palpable or tender. Two definite spider angiomas were visible, one on the neck and one on the left shoulder; one showed blanching on pressure. On March 25 no changes were noted, except that both spider angiomas were slightly less distinct, but they were still noticeable; neither showed blanching on pressure. Physical examination on August 8 showed two small red spots still visible at the site of the spider angiomas; they no longer had the shape of a spider and did not blanch on pressure.

CASE 3. On November 25, 1945, this 6-year-old boy developed a moderate diarrhea that was followed by considerable pain and tenderness in the right upper abdomen. Some nausea and anorexia were present but no vomiting. No jaundice was noticed. He recovered uneventfully except for slight pain over the liver area that persisted for several weeks. He stayed out of school for 3 days because of illness.

Physical examination on January 26, 1946, showed that the liver and spleen were not palpable or tender. Seven definite spider angiomas were found over the arms and shoulders; four of them blanched on pressure. Determinations of bromsulfalein retention and plasma bilirubin were normal. The thymol-turbidity values were as follows: on January 26,

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11 units; on February 20, 10 units; on March 25, 6 units; and on August 8, 4 units.

On March 25 the liver and spleen were not palpable or tender. Five of the seven spider angiomas were still present, but they had faded considerably; only one blanched on pressure. On August 8 two small spider angiomas were still visible; one blanched on pressure. Red spots remained at the sites of two old spider angiomas.

CASE 4. On December 22, 1945, this 15-year-old boy developed nausea, anorexia and vomiting, which lasted for 2 days. He also complained of soreness over the abdomen and of nosebleeds. He continued to go to school, however. Recovery was uneventful except for persistent soreness over the abdomen that caused him to bend over slightly as he walked. No jaundice was noticed.

Physical examination on January 26, 1946, revealed the liver edge to be just palpable on deep inspiration and slightly tender. The spleen was not palpable. No spider angiomas were observed. The bromsulfalein retention and plasma bilirubin were normal.

On March 25 the liver and spleen were not palpable or tender, and there were no spider angiomas.

The thymol-turbidity values were as follows: on January 26, 13 units; on February 20, 11 units; and on March 25, 5 units.

CASE 5. On January 12, 1946, this 17-year-old boy developed a headache associated with chills and fever. This was followed by nausea, anorexia and an episode of vomiting. The acute symptoms lasted approximately 1 week. Other symptoms included soreness over the liver area, hives, itching of the skin, marked fatigue, somnolence, clay-colored stools and a weight loss of 12 pounds. Jaundice was noticed on January 20, 4 days after the onset of dark urine. Recovery was uneventful except for liver tenderness, which persisted for approximately 3 weeks.

Physical examination on January 25 revealed the liver to be palpable two fingerbreadths below the costal margin and definitely tender. The spleen was not palpable. A definite spider angioma was noted over the anterior portion of the neck.

On March 25 the liver was not palpable or tender, and the spleen was not palpable. The spider angioma had almost disappeared but could still be found. On August 8 the spider angioma had completely disappeared.

The liver-function tests were as follows:

DATE	PLASMA BILIRUBIN	BROMSULFALEIN RETENTION AT 45 MINUTES	THYMOL TURBIDITY
	mg./100 cc.	%	*units*
January 26	2.8	27.5	14
February 1	1.1	3.5	17
March 25	0.8	2.0	8
August 8	0.7	3.0	5

CASE 6. On January 20, 1946, this 12-year-old boy developed a slight loss of appetite and a feeling of malaise. Two days later jaundice was noticed, and he was admitted to the hospital. The jaundice was slight and rapidly disappeared. The liver and spleen were never palpable or tender, and no spider angiomas were observed. The patient made an uneventful recovery.

The liver-function tests were as follows:

DATE	PLASMA BILIRUBIN	BROMSULFALEIN RETENTION AT 45 MINUTES	THYMOL TURBIDITY
	mg./100 cc.	%	*units*
January 24	3.5	46	14
January 30	3.0	37	19
February 6	0.9	6	18
February 17	0.6	3	10
April 23	—	—	3

CASE 7. On January 21, 1946, this 20-year-old girl developed nausea and anorexia associated with a mild fever. This was followed by moderate abdominal pain and a feeling of fatigue. Jaundice was noticed on January 25, and she was admitted to the hospital.

Physical examination disclosed marked liver tenderness; the liver was palpable three fingerbreadths below the costal margin. The spleen was also palpable. No spider angiomas were observed. The patient showed rapid improvement on bed-rest therapy. The liver tenderness persisted for 2 weeks after admission. Recovery was uneventful.

The liver-function tests were as follows:

DATE	PLASMA BILIRUBIN	BROMSULFALEIN RETENTION AT 45 MINUTES	THYMOL TURBIDITY
	mg./100 cc.	%	*units*
January 25	5.0	48	17
January 29	7.0	40	28
February 5	1.4	6.0	20
February 11	0.8	2.0	21.5
February 19	0.6	1.0	12.3
February 26	0.4	2.0	9.5
March 6	0.5	1.0	6.7
March 13	0.5	1.0	6.3
April 7	0.4	1.0	5.9
April 23	0.2	2.0	4.0

CASE 8. On January 24, 1946, the mother noticed that this 3-year-old girl had lost her appetite. The temperature was 101°F. On the following day the patient was seen at the hospital.

Physical examination revealed no evidence of jaundice. The liver and spleen were not palpable or tender. The temperature was 100°F. The patient regained her appetite 2 days later, and no further signs or symptoms were demonstrable.

The liver-function tests were as follows:

DATE	PLASMA BILIRUBIN	BROMSULFALEIN RETENTION AT 45 MINUTES	THYMOL TURBIDITY
	mg./100 cc.	%	*units*
January 25	0.5	13.5	9.0
February 2	0.2	1.0	13.0
March 25	0.3	2.0	7.0
August 8	0.4	2.0	4.0

CASE 9. On February 8, 1946, this 13-year-old boy noticed a slightly sore throat. His mother found the temperature to be 104°F. The patient had a slight headache and a decrease in his appetite at this time but no nausea or vomiting. He was admitted to the hospital 24 hours after the onset of symptoms.

Physical examination showed that the liver and spleen were not palpable or tender. There were no spider angiomas and no icterus. The throat was somewhat reddened. A throat culture was negative. The temperature was 103°F. but fell to normal 12 hours after admission. Anorexia persisted for 2 days. The liver and spleen never became palpable or tender. On February 10 the patient developed a large spider angioma on the right side of the neck that had not been present on admission and another small one over the right shoulder. These showed gradual fading over a 4-month period of observation. Careful observation also revealed a slight yellow tinge to the scleras on February 15, which disappeared rapidly. Recovery was uneventful.

The liver-function tests were as follows:

DATE	PLASMA BILIRUBIN	BROMSULFALEIN RETENTION AT 45 MINUTES	THYMOL TURBIDITY	CEPHALIN FLOCCULATION
	mg./100 cc.	%	*units*	
January 26	0.4	2.5	0.5	0
February 8	0.6	30	3.5	++
February 11	1.0	31.5	12.5	++
February 13	2.3	34.5	16.3	++
February 18	1.3	11.5	21.5	++
February 25	0.5	3.0	22.7	+++
March 5	0.6	1.2	15.5	++
March 12	0.4	2.0	13.5	++
March 26	0.35	1.5	7.0	0

EPIDEMIOLOGY

The origin of the outbreak was not completely certain. One member of the family (M. G.) had been stationed at a naval base in Virginia at a time when a number of cases of infectious hepatitis were occurring. Approximately a month prior to the first case in the family, he came home on five days' leave. During that time he became ill with symptoms of nausea, dizziness and fever; he remained in bed at home for three days. No jaundice was noticed by

his mother, and he returned to duty at the end of his visit feeling well. No further information could be obtained. In the light of later developments, it seems possible that he had a light attack of infectious hepatitis and transmitted it to other members of the family. No known cases of jaundice had occurred in the community in recent years prior to the first case in this family.

The sequence of events may best be followed by a division of the outbreak into six parts (Fig. 1). In tenement house. This consisted of a kitchen and bedroom connected by a hallway that was broken up into three small bedrooms (Fig. 2). A small bathroom and toilet opened into the kitchen. The most striking feature of the apartment was the close proximity of the seven beds in the hallway and bedroom. Two children slept in each of four of the beds, and there was considerable variation in occupancy. The father worked at night and slept during the day in any bed that was not occupied when he returned

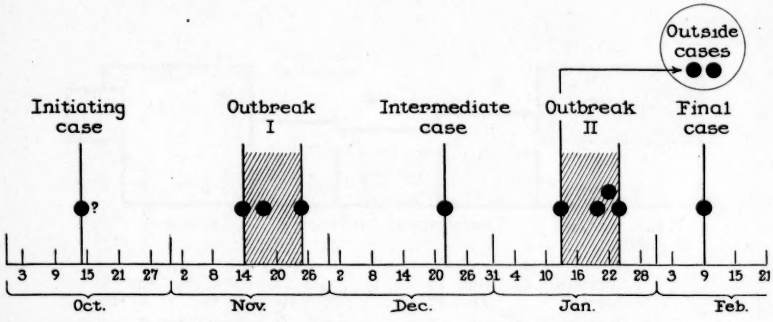

FIGURE 1. *Time Relation of the Cases of Infectious Hepatitis in the Family G. Epidemic.*

October M. G., who was probably the origin of the epidemic, became ill at home while on leave from the Navy. In November, 3 siblings became ill. A month later a single case occurred in the family. In January, 4 new cases appeared in the family. And in February a single case occurred in the family and 2 cases appeared in friends of E. G. (Case 5).

This epidemic was not investigated until the beginning of the second outbreak in the family. The diagnosis of infectious hepatitis in the cases of the first outbreak was made on the basis of a characteristic symptomatology corroborated by at least one persistent finding, such as liver tenderness, spider angiomas or abnormalities in liver-function tests. In the other cases, which were followed throughout the course of the disease, the diagnosis was definite because of the presence of jaundice or marked aberrations in two or more liver-function tests. Six patients in the family did not show jaundice. Only 1 child and the parents demonstrated no evidence of the disease, although they were examined and tested on several occasions. This epidemic, therefore, represented 9 cases of infectious hepatitis among the children of the family and 2 cases among friends of one of the children.

The home conditions were inadequate for such a large family. The 10 children and their parents lived in a moderately small apartment in an East Side from work. The sheets on the beds were changed every two weeks. Except for the crowded condition of the beds, conditions in the apartment were good. The children were kept clean, and the mother was careful with the food. The family was healthy, and no illnesses besides the usual childhood diseases had ever appeared.

Several epidemiologic studies on infectious hepatitis have been reported in which the spread of the disease was related to contact in sleeping quarters.[13–15] In the outbreak under study, it is difficult to escape the conclusion that the crowded sleeping quarters were in some way responsible for the high incidence of cases.

An approximation of the length of the incubation period of the disease in this epidemic can be gathered from the fact that two friends of one patient (Case 5) developed the disease twenty-six and twenty-eight days respectively after he became ill. These friends had had no contact with any other members of the family and had not been near any other known cases of infectious hepatitis. They saw the patient only at a boys' club to which none of the other members of the family belonged; their contact was fairly close, and they admitted the possibility of an interchange of a single cigarette while the three of them, together with several others, played pool. The patient attended the club during the night prior to the onset

of symptoms and then stayed away for two weeks because of illness; twenty-seven days is therefore the probable incubation period, although the possibility exists that he may have infected them several days prior to the onset of his own illness. The close relation in the time of occurrence in these 2 cases adds validity to the assumption of such an incubation period.

The 10 children of the family who were at home lived under conditions that required the closest contact. They all ate together around a very small table; they all used the same small bathroom; and, under the crowded conditions that existed in the apartment, they practically all slept together. The older children washed and cared for the younger ones. It is to be expected that a contagious infection would spread with ease and rapidity through such a group. At least 9 of the children were susceptible to the disease, as shown by the fact that they eventually became ill. The infection, however, did not spread rapidly through the family. Three children became ill over a period of ten days in November. They probably contracted the disease from their sailor brother, who had been ill at home approximately a month earlier. Six susceptible children failed to develop the disease at that time, although they were in equally close contact with him.

In December, 29 days after the last case of the November outbreak, one boy developed the disease. He must have contracted the infection from one of the children of the November outbreak, if the incubation period is at all close to the estimated twenty-seven days. Five susceptible children failed to contract the disease from the 3 children with whom they lived every day during their illness in the November outbreak.

In January, 4 children developed infectious hepatitis over a period of twelve days — approximately a month after the single case in December. They must have contracted the disease from this patient who kept the infection alive in the family between the November and January outbreaks.

Finally, in February, another boy became ill with the disease. He must have obtained the virus from one of the January group after escaping three previous periods when others in his family had become infected.

One of the children apparently never contracted the disease, although he was exposed fully as much as the others in his family. The possibility remains, however, that he had a subclinical infection.

The question why the parents did not come down with infectious hepatitis is a slightly different one. They were exposed to the virus in each of the outbreaks fully as much as the children. Neither gave a past history of jaundice. If they were as susceptible as the children, the chances would have been 100:1 that at least one of them would contract the disease. The lack of susceptibility to the disease of older people has frequently been noted. Immunity as a result of mild unnoticed infection with the disease earlier in life has been offered as a possible explanation.

This serial spread in families has been noted by Pickles[2] and Newman[3] and is without counterpart in any other disease. That infectious hepatitis is not

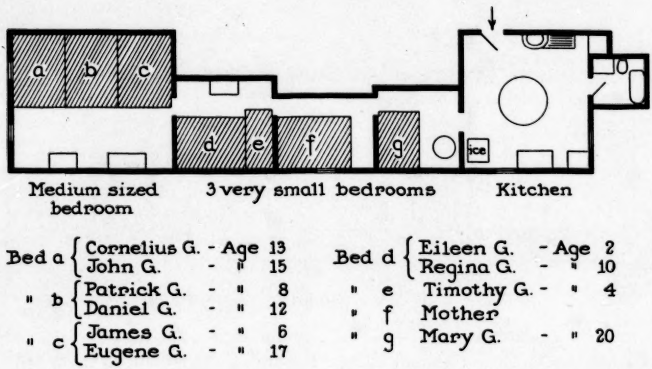

FIGURE 2. *Plan of the Apartment of Family G.*

extremely contagious is evident from this type of spread. The demonstration of subclinical infections, missed infections and carrier states adds strength to the idea that the disease is usually spread by contact. In the outbreak under consideration, only 5 of the 11 patients showed jaundice. Diagnosis of infectious hepatitis in 2 cases was made by means of liver-function tests alone in the absence of signs or symptoms characteristic of the disease; these are discussed below. There was definite evidence of the existence of cases that might have been missed under ordinary conditions. The chain of events in the

Liver-Function Tests

Following a study of various tests of liver function in acute hepatitis among Navy personnel at the Rockefeller Hospital, the conclusion was reached that the condition of the patient could best be evaluated by the determination of the plasma bilirubin, the bromsulfalein retention and the thymol turbidity.[16] The use of these tests in the epidemic described above offered further information regarding their comparative significance and showed their value in the detection of cases without

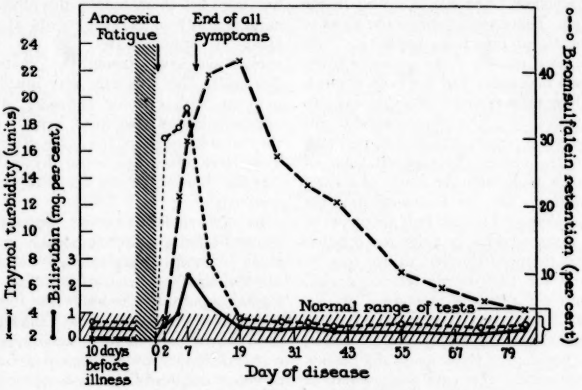

Figure 3. *Comparative Results on Serial Determinations of Plasma Bromsulfalein Retention, Plasma Bilirubin and the Thymol Turbidity Reaction of the Serum in Cornelius G. (Case 9).*

epidemic would not have been evident if sole reliance had been placed on the presence of jaundice.

Recent studies on poliomyelitis have shown the presence of virus in the stools of people who have had close contact with the disease and who never showed evidence of infection. They undoubtedly act as carriers. This state of affairs has not as yet been demonstrated in infectious hepatitis, although the virus is present in the feces of certain patients suffering from the disease. One cannot help remarking that the epidemiology of the two diseases has many similarities. In the family under discussion the contact between the children was extremely close, and spread by fecal contamination seems likely. Mild cases of infectious hepatitis other than those found in this epidemic must exist, and these, together with probable carriers of the virus, may explain the apparent absence of contact between cases that has often been noted and used as an argument against contact as a significant agent in the spread of the disease.

jaundice. The thymol-turbidity test was found to have special use in the epidemiologic study.

Figure 3 presents the results of serial determinations in Case 9. Because of illness in his siblings, this patient was examined ten days prior to the onset of his own illness, and normal values for the various liver-function tests were found. This gave added significance to the changes produced when the disease began. It can be seen that the bromsulfalein retention became elevated within twenty-four hours after the onset of the first symptoms. Values for the plasma bilirubin did not begin to rise until the fifth day, reaching a peak on the seventh day of the disease. This peak corresponded with that of the bromsulfalein retention, and values for the two tests rapidly returned to the normal range. The curve of serial determination of the thymol-turbidity test, however, showed a delayed rise reaching a peak on the nineteenth day of the disease at a time when the other two tests had fallen to normal and the patient was free of symptoms. The thymol-turbidity values

then fell slowly, reaching the normal range on approximately the nineteenth day of the disease.

The other cases in the family that were studied also bore out the findings that the bromsulfalein retention demonstrates an immediate increase with the onset of symptoms during the preicteric stage and that the thymol-turbidity values show a delayed rise and prolonged elevation persisting well after the end of all symptoms of the disease.

Despite these marked abnormalities in liver-function tests the patient in Case 9 had only minor symptoms, consisting of mild anorexia, sore throat and slight fatigue. No definite jaundice was ever visible, and it was only by extremely careful observation that a slight yellow tinge was observed in the scleras on one day. There were none of the signs or symptoms diagnostic of infectious hepatitis. This case would have been missed if the sensitive liver-function tests described above had not been applied.

The value of these tests as diagnostic aids was also demonstrated in Case 8. This three-year-old girl developed a loss of appetite, which was reported by her mother only because the slightest signs of illness were looked for following the illness of several of the other children. On the following day the bromsulfalein test showed 12.5 per cent retention of the dye, and the thymol-turbidity value was 9 units. Subsequently, the thymol-turbidity values rose to a peak of 13 units and then slowly fell to normal, and the bromsulfalein retention remained within the normal range. The patient developed no further symptoms, the liver was never palpable or tender, and there was no jaundice or elevation of the plasma bilirubin. The pattern in this case was similar to that in Case 9, with an immediate rise and rapid fall of the bromsulfalein retention associated with a delayed rise and prolonged elevation of the thymol reactivity of the serum. The combination of these tests made possible the diagnosis of an extremely mild case of infectious hepatitis.

Several members of the family were seen just after the symptoms of infectious hepatitis had subsided, when the plasma bilirubin and bromsulfalein retention were normal. The thymol-turbidity test, however, still revealed elevated values that fell slowly to normal over a period of several weeks. The use of this test made it possible to confirm the diagnosis of infectious hepatitis after the patients had apparently recovered from the disease. The patient in Case 3 illustrates this point. He developed nausea, anorexia, pain over the liver area and diarrhea lasting for three days. Moderate fatigue and liver pain persisted for several weeks. No jaundice was noted. When he was first seen two months after the onset, he had no complaints, and physical examination was negative. Determinations of plasma bilirubin and bromsulfalein retention were normal. The thymol reactivity of the serum was still positive at 11 units, and this gradually fell to 4 over a period of several months. The symptoms of the acute attack were characteristic of infectious hepatitis, and the thymol-turbidity test confirmed the diagnosis. Thus, it can be seen that this test is of value in an epidemiologic study not only because of its aid in the diagnosis of nonicteric cases but also because it remains positive for such a long period, revealing significant data after other evidences of the disease have disappeared.

Occurrence of Spider Angiomas

Spider angiomas in the acute stage of infectious hepatitis have occasionally been described,[17, 18] but little emphasis has been placed on their occurrence. Most clinical descriptions of the disease do not even list them among the physical signs. In a clinical study of Navy patients at the Rockefeller Hospital, approximately 30 per cent developed spider angiomas during the acute stage of the disease.[19] The incidence was much higher among patients with chronic hepatitis, and new spider angiomas usually signified a poor prognosis when they developed after the acute stage of the disease. They have served as a useful physical sign for following the transition from acute to chronic infectious hepatitis.

In the epidemic under discussion 5 children showed definite spider angiomas, and their presence aided in confirming the diagnosis of the disease in some of the cases without jaundice. Case 9 offered a good opportunity to study the formation and disappearance of the angiomas. The patient was examined ten days before the illness, and a search was made for spider angiomas because of their presence in his siblings; none were found. Twenty hours after the onset of the first symptoms he was again examined, and none were found. On the following day, however, he was discovered to have developed during the night a large angioma located over the lower right side of the neck and a considerably smaller one on the right shoulder; both blanched readily on pressure. They were carefully observed for a six-month period, during which a gradual fading took place. During the second month the quality of blanching on pressure disappeared. At the end of six months, the smaller one had completely disappeared, and the larger was visible only as a small, barely discernible, red speck. These marks, however, could still be identified as spider angiomas at the end of four months, long after the illness had terminated.

In Case 3 seven definite spider angiomas developed over the arms and shoulders. The mother noticed their appearance at the time of the acute symptoms, and the angiomas were still present when the patient was first seen in the clinic two months later. They stood out more plainly against the background of his smooth, white skin than they would have in an adult. These spider angiomas faded slowly, and two could still be identified at the end of eight months, although the patient had no persistence of signs or

symptoms of the disease. Their presence confirmed the diagnosis of infectious hepatitis.

Next to liver tenderness spider angiomas proved to be the most useful physical sign in the study of the cases in this epidemic. They were of special value in the patients whose illnesses had begun before the investigation and in whom the diagnosis was not definite from the description of the acute symptoms. Their long persistence following a short, mild attack of infectious hepatitis was somewhat unexpected. It suggests the possibility that the so-called "spontaneous spider angiomas" in normal persons occasionally result from a mild attack of infectious hepatitis without jaundice. In this group of children 4 of the 5 cases showing spider angiomas were so mild that jaundice was not seen. Another point that should be raised is that the persistence of the angiomas could not be explained on the basis of a lingering hepatitis. These children all recovered rapidly and uneventfully from the acute attack. The significance of persistent spider angiomas in chronic hepatitis and cirrhosis should be evaluated in the light of these findings.

Incidence of Infectious Hepatitis without Jaundice

The existence of nonicteric cases of infectious hepatitis is now clearly recognized, but there is no agreement about the number of such cases. Various estimates for the percentage of nonicteric cases have been given: 9 per cent (Bates[20]); 50 per cent (Barker et al.[21]); 27 per cent (Neefe and Stokes[8]); 22 per cent (Hardy and Feemster[22]); and 89 per cent (Gowen[23]). Undoubtedly, the percentages vary with the epidemics. A possible reason for the marked divergence noted is that each group of patients was studied in a different manner. The high incidence obtained by Gowen[23] in Tunisia is due to the fact that he estimated the icteric index in a large number of persons and considered an abnormal value as indicative of a case of infectious hepatitis. The lack of corroborative evidence opens his findings to some question. In the family epidemic reported above 6 children had infectious hepatitis without jaundice — an incidence of 66 per cent.

Table 1. *Relation of Age to the Occurrence of Jaundice.*

Case No.	Age	Jaundice
	yr.	
7	20	++++
5	17	++++
4	15	0
9	13	0
6	12	++
1	10	0
2	8	0
3	6	0
8	3	0

Age seemed to be an important factor in the determination of the severity of the illness and the presence of jaundice in the members of this family. The mildest case occurred in Case 8, in which the patient was the youngest of the family, and the severest case occurred in the oldest patient (Case 7). Table 1 presents the age distribution in relation to the occurrence of jaundice, and it is evident that jaundice occurred more frequently in the older age group.

Summary

The serial occurrence over a period of five months of 9 cases of infectious hepatitis in a single family is described.

Contact was found to be the probable mode of spread in this outbreak.

Determinations of bromsulfalein retention and thymol reactivity of the serum proved to be valuable aids in the detection of nonicteric cases.

The thymol-turbidity test, because of its prolonged elevation, was of special value in an epidemiologic study.

Spider angiomas, which developed during the acute attack of infectious hepatitis, were found in 5 cases. The sudden onset and delayed disappearance of this physical sign are described. It proved to be helpful in corroborating the diagnosis in 2 cases.

Six children did not develop clinical evidence of jaundice.

The severity of the illness and the presence of jaundice showed a definite relation to the age of the children, the disease being milder in the younger group.

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MASSIVE GASTROINTESTINAL BLEEDING FOLLOWING EXPOSURE TO LOW PRESSURE

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In recent years reports of gastrointestinal hemorrhage from obscure and comparatively rare origins have been accumulating. Hematemesis is an exceedingly dramatic episode for the patient, and melena is equally so for the physician. After gastric or duodenal ulcer, varicosities of the esophagus and rectum or carcinoma of the stomach and large bowel have been dismissed, a diagnostic impasse is reached. This paper is the result of such a situation. No attempt is made to present an inclusive differential diagnostic study, but the possibilities of various lesions of more infrequent occurrence are considered. McBurney has been quoted as saying, "Deliver me from the man of one case." Nevertheless, the following single case report is presented as a diagnostic problem.

Case Report

On October 2, 1943, a 29-year-old medical officer was admitted to a station hospital because of bloody diarrhea of 2 days' duration.

The past history was not remarkable except for a strong family and personal history of allergy. On one occasion 4 months previously, the patient had noted several purpuric spots on the forearms preceding a flareup of chronic neurodermatitis. In 1942 a tonsillectomy and adenectomy had been done without complication. A system review was noncontributory.

Two days before admission the patient had been exposed to a simulated altitude of 41,000 feet while demonstrating some of the phenomena of high-altitude physiology. He had felt well before entering the low-pressure chamber where this demonstration had taken place and had taken no medication except for 0.25 per cent Neosynephrine nose drops to alleviate symptoms of hay fever and to prevent aero-otitis. In addition, he had drunk a bottle of Coca-Cola before entering the chamber.

In a period of 20 minutes, pressure in the chamber was reduced from that of the ground level, approximately 12 pounds per square inch, — equivalent to 4280 feet above sea level, — to 2.6 pounds per square inch — equivalent to an altitude of 41,000 feet. During the reduction in pressure, the patient had crampy abdominal pain with distention. This was mild at first but increased during the 10 minutes at that pressure. The pressure was then increased to 2.75 pounds per square inch — equivalent to an altitude of 39,000 feet. This was maintained for ½ hour. The abdominal pain was not disabling but was definitely uncomfortable. It was relieved on return to ground-level pressure, the transition occupying 15 minutes; at that time the patient felt well. The abdominal pain disappeared during the increase in pressure.

He ate a good supper and went to bed early and to sleep quickly. About 4 hours after retiring he was awakened with crampy abdominal pains that were generalized and associated with a desire to evacuate. A large bloody diarrhea containing dark clots ensued. Three hours later similar rectal bleeding occurred. The next day the patient felt well and went about his daily duties. Three more stools, however, in the next 24 hours, more formed in character but tarry, brought him to the hospital.

The chief complaint on admission was a feeling of fatigue and muscular weakness. Physical examination was negative except for pallor of the skin, congestion of the nose and a tarry stool on rectal examination.

The temperature was 98.6°F., the pulse 92, and the blood pressure 124/78.

Examination of the blood revealed a red-cell count of 4,300,000, with a hemoglobin of 13 gm.; during the day the red-cell count fell to 3,500,000, with a hemoglobin of 12 gm. (On the day before admission, the red-cell count had been 5,070,000.) The nonprotein nitrogen was 32 mg. and the blood sugar 115 mg. per 100 cc., and a blood Kahn test was negative. The urine was a clear amber, with a specific gravity of 1.026, negative for albumin and glucose and microscopically normal.

On the 2nd day the patient felt better in the morning. The blood pressure was 122/78, and the pulse 90; the abdomen was soft without masses or tenderness. Toward evening the abdomen became distended, and the oral temperature rose to 99.0°F., and the pulse to 142. The red-cell count was 3,080,000, with 9 gm. of hemoglobin and abundant platelets. The bleeding time was 90 seconds, and the clotting time (capillary tube) 45 seconds; the tourniquet test was negative. The white-cell count was 8200, with 70 per cent segmented and 2 per cent nonsegmented neutrophils, 24 per cent lymphocytes, 2 per cent monocytes, 2 per cent basophils and no eosinophils. A transfusion of 400 cc. of Type A citrated blood was given without reaction.

On the 3rd hospital day the stools were reported negative for ova and parasites and nonlactose fermenting bacteria. The abdomen was less distended; the skin was pale, and the patient was comfortable but feeling much more lassitude. The diet was a modified Meulengracht regime with feedings of puréed food every 2 hours. The appetite was poor. Amphojel and lime water were given between feedings. That evening a 600-cc. transfusion was given without reaction. The temperature had been rising throughout the day and had reached 103°F. before the transfusion was begun. It fell slowly to normal in the next 36 hours and was accompanied by a fall in pulse.

On the 5th hospital day the stools became normal in appearance but remained guaiac positive. The patient was given a normal diet at that time.

On October 11 a proctoscope was introduced to its full distance of 25 cm. without difficulty. The mucosa of the sigmoid and rectum appeared entirely normal. There were no tumors or areas of ulceration and no bleeding points. A small internal hemorrhoid was not believed to account for the bleeding.

On October 12 preliminary fluoroscopy of the chest was entirely negative. Examination of the large bowel showed no evidence of intrinsic organic disease. The terminal ileum filled and appeared normal; the appendix was partially filled. X-ray films made with the colon filled and after the evacuation of the barium, as well as contrast films after evacuation, failed to demonstrate any lesion within the large bowel.

On the following day preliminary chest fluoroscopy was again entirely negative. The esophagus was normal. The stomach was hyperactive, with deep regular peristaltic waves and rapid gastric emptying. The duodenal cap filled out well and showed no defects and no evidence of irritability. The duodenal loop appeared normal. Serial films of the small bowel made at hourly intervals disclosed no abnormality in the distribution of the barium meal.

On October 15 the patient was placed on a meat-free diet for 48 hours. The stools gave a ++ guaiac reaction but were guaiac negative 2 days later, when the patient was discharged. Examination of the blood at that time showed a red-cell count of 4,000,000, with 12 gm. of hemoglobin. The patient was given a month's sick leave before resuming his regular duties and advised to continue amphojel, to avoid strenuous exercise and to have an x-ray checkup examination on return to duty.

One month after admission careful x-ray examination of the esophagus, stomach and duodenum was negative. Eighteen months later the stools were negative for occult blood on a

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meat-free diet, and the patient was asymptomatic. Further x-ray studies of the esophagus, stomach and small bowel revealed no abnormality.

Discussion

The possible relation of the bleeding to the exposure to low pressure is interesting. The character of the bleeding was such that it resembled a slow oozing over a period of nearly a week — it was not the sudden rush and exsanguination typical of a bleeding ulcer. It could be said that the relation of this bleeding to the exposure to low pressure was purely fortuitous. The short time between the two events is a persuasive reason for believing that the bleeding was the result of the exposure to the low pressure. In addition, the association of the abnormally severe crampy abdominal pains with the exposure to low pressure is another reason for considering the bleeding related to the latter event. The patient had had an uneventful simulated flight nine months previously to 39,000 feet for thirty minutes. Ordinarily, some abdominal distention and slight abdominal cramps can be expected on exposure to low pressure, but the symptoms were severer and associated with an inability to pass flatus, which ordinarily relieves the mild abdominal distress.

Gas saturated with moisture and at a constant temperature can be calculated to expand about six and a half times under the conditions that the patient experienced. Because of the reduction in the partial pressure of oxygen, the breathing of 100 per cent oxygen at 33,700 feet is comparable to the breathing of air at sea level. At 41,000 feet, in spite of the breathing of 100 per cent oxygen, experiments at the Aeromedical Laboratory at Wright Field showed that the blood is approximately 85 per cent saturated with oxygen. This slight anoxic state may be enough to increase the effects of any trauma to capillary blood vessels.

During the course of the war, many men were processed in low-pressure chambers. The Air Surgeon's Office reports that 470,592 simulated altitude flights were made, ordinarily including 3 flights per person, and that during the course of the flights only 6 fatal cases traceable to this experience occurred.[1]

It is not the intent of this paper to discuss the reasons for these fatalities. But a brief review of the autopsy protocols in 2 cases may be of interest. The subjects showed pulmonary edema, which appeared on the average about four hours after exposure and was the immediate cause of death. None of the patients gave a history or allergy. Two patients showed gross and microscopical hemorrhage into the gastrointestinal tract.

Case 4. This officer had been exposed to a simulated altitude of 30,000 feet for 1 hour. Post-mortem examination showed the serous surface of the entire gastrointestinal tract to be smooth and free of exudate. The serosal vessels appeared congested. No subserosal hemorrhages were seen. The stomach contained about 200 cc. of brownish fluid. Scattered over the mucosa of the stomach and duodenum were numerous areas of hemorrhage. These were dark red and appeared to be of recent origin. They measured from 0.3 to 3 cm. in diameter. The first 90 cm. of the jejunum appeared normal. The mucosa of the remaining portion of the jejunum and all except the terminal 60 cm. of ileum showed what appeared to be a diffuse confluent hemorrhagic necrosis. The mucosa was dark red. The lumen of the small intestine contained a moderate amount of reddish-black fluid. The small and large intestines were not distended. The mucosa of the colon showed no lesions. The lumen of the colon contained a moderate amount of yellow, soft fecal material. The appendix was not abnormal.

Microscopical examination revealed marked mucosal hemorrhage of the stomach and small intestine. The mucosa of the stomach showed slight autolytic changes; no other pathologic changes were noted. The mucosa of the duodenum had undergone slight autolysis. A section of mucosa from the small intestine disclosed some autolytic changes. One section from the site of hemorrhage showed the villi to be hemorrhagic, and blood cells were scattered throughout the connective tissue. The mucosa was covered with material consisting of red cells. The mucosa of the colon was intact, and only minimal pathologic changes were seen.

The anatomic diagnoses were acute pulmonary edema, pleural effusion and extensive capillary damage to the mucosa of the stomach and small intestine.

Case 5. A private had been exposed to an altitude of 30,000 feet for 30 minutes. Post-mortem examination revealed no abnormalities in the stomach. The small bowel showed prominence of Peyer's patches in the vicinity of the ileocecal valve and 45 cm. proximal to it. Scattered hemorrhagic streaks were observed throughout the small bowel, especially in the duodenum and the jejunal area.

The anatomic diagnoses were laceration of the dura and herniation of the brain (left parietal lobe), with congestion and edema of the brain tissues, marked pulmonary edema and extensive congestion of both lungs and scattered hemorrhages in the small intestine.

Two possibilities exist to explain the hemorrhages. The first is that the morphologic changes were a result of the profound shock that accompanied the fatal cases. Erlanger and his associates[2] and later Moon[3] described the distinctive circulatory changes in shock that correspond to the gross and microscopical picture presented in these fatal cases.

The second possibility, which is theoretically plausible, is that air emboli developed in the distended capillary network of the bowel where the circulation was impeded. The mechanical distention from the formation of air emboli caused disruption and increased permeability of the capillary endothelium. It does not seem likely that the slight systemic anoxia, which was undoubtedly present in the case presented above, was in itself sufficient to cause hemorrhage, but conditions in the bowel may have aggravated the local anoxia that was present.

This first possibility may well apply to the fatal cases but not to the case reported above, for at no time did the patient give evidence of being in shock. It can safely be assumed that the bleeding in that patient was below the level of the pylorus, for it is infrequent that a gastric lesion is not associated with hematemesis.

Inquiries addressed to the Committee on Medical Research of the Office of Scientific Research and Development led to a reply from Dr. Kenneth B. Turner,[4] chief of the Record Section, who did not recall having heard of a previous example of mas-

sive intestinal bleeding following exposure to low pressure.

Dr. John F. Fulton,[5] chairman of the Subcommittee on Decompression Sickness, National Research Council, reported that he had observed no cases of gross hemorrhage following exposure to high altitudes.

Causes to be considered other than anoxia and distention are a Meckel's diverticulum, allergy and primary tumor of the small intestine.

In 1808 Willan in his book *Cutaneous Disease* mentioned the relation of anasarcous lesions of the thighs and hands, presumable angioneurotic edema, associated with purpura, vomiting, abdominal pain, diarrhea and bloody stools. This was described more fully by Henoch in 1874, and the symptom complex was given his name. Sir William Osler[6] presented several cases of purpuric and sometimes merely erythematous skin lesions associated with visceral lesions, particularly gastrointestinal bleeding.

The allergic background in the case presented above makes Henoch's purpura a possibility, but the single occurrence of bleeding and the older age group make this possibility less probable. An adequate follow-up study was not possible for the full evaluation of other possibilities. Esophagoscopy and gastroscopy might have been helpful. Early x-ray films would have been desirable after this massive gastrointestinal hemorrhage, and postponement of such examination may be the reason why no lesion was found.

Cases of undiagnosed gastrointestinal bleeding are common to the experience of every doctor, but not frequent enough for generalization from his personal experience. Stone[7] presented 72 cases of massive melena of obscure origin, in 31 of which no cause could be ascribed; 6 of these patients were subjected to celiotomy — one on two occasions — without further elucidation of the etiology. Even at post-mortem examination of subjects with cirrhosis of the liver, esophageal varices are often demonstrated only with great difficulty although death followed sudden hematemesis.

Congenital diseases must be considered as causes of intestinal bleeding. Autopsy studies reveal that Meckel's diverticulum occurs in about 2 per cent of the population and three times as often in males as in females. The diverticulums often contain heterotopic gastric mucosa or pancreatic tissue that is subject to ulceration.[8, 9] The symptoms often simulate peptic ulcer both in periodicity of pain and in bleeding. X-ray films of the small intestine do not contribute definitive information, and in the presence of questionable roentgenographic findings, a presumptive diagnosis of peptic ulcer is often made. The failure of x-ray examination to outline Meckel's diverticulums is probably a result of their usual structure. Typically, the orifice is relatively large with a small lumen. The diverticulum is short; consequently, barium enters easily and leaves promptly. In addition, overlying masses of small bowel may obscure diverticulums that do remain filled. In fact, x-ray visualization is considered something of an achievement.[10]

Primary tumors of the small intestine are rare but are frequently associated with bleeding, intussusception and pain. Rankin and Mayo[11] list 31 cases of small-bowel carcinoma seen during the same interval in which 2646 cases of cancer of the stomach and 2775 of the large bowel and rectum were seen. Klingenstein[12] describes 2 cases of benign lesions of the small intestine complicated by severe hemorrhage. Benign tumors occur about half as frequently as the malignant variety. Segal, Scott and Watson[13] presented a case of carcinoma of the jejunum in which the patient exsanguinated to a hemoglobin level of 6 gm. The carcinoma was a 3-mm. nodule in the center of which was an area of ulceration. In the case presented above tumor seems unlikely because bleeding has not recurred in nearly three years.

In cases of massive gastrointestinal hemorrhage treatment for the loss of blood is, of course, of paramount importance. Early x-ray study seems advisable if the roentgenologist is cautioned to avoid kneading the abdomen. Under these circumstances, there can be little objection to x-ray examination except when the possibility of intestinal obstruction is present. Esophagoscopy and gastroscopy are recommended as part of the complete examination. Blood studies to eliminate certain purpuras as etiologic factors are necessary.

Stone[7] emphasizes the fact that premature surgery should be avoided. It is quite possible that patients who have bled only once will bleed no more. When the source of bleeding is definite, surgery is indicated. In the cases that seem completely unexplained and in which the hemorrhages are severe and recurrent, operation is the recourse of desperation and bafflement. Such intervention may fail to discover or to relieve the difficulty.

Summary

A case of severe intestinal hemorrhage associated with exposure to low pressure during simulated high-altitude flight is presented. The differential diagnoses are discussed, and possible etiologic factors reviewed — namely, shock, acute dilatation and air embolism of the bowel and increased capillary permeability associated with an allergic diathesis.

Other possible sources of bleeding of an obscure nature are discussed, including Meckel's diverticulum and new growths of the small intestine.

Treatment is symptomatic, with early transfusion. After the bleeding has been controlled, diagnostic procedures can be considered. Surgery is indicated when the source of the bleeding is definite and the lesion is remediable by surgery or when severe

recurrent hemorrhages of unknown nature leave surgery as the only resort.

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MEDICAL PROGRESS

PEDIATRICS (Concluded)*

MEMBERS OF THE STAFFS OF THE CHILDREN'S AND INFANTS' HOSPITALS†

BOSTON

Attitudes toward Infant Care

The care of infants is largely influenced by physiologic and psychiatric knowledge, much of which has accumulated in the past few years. Fundamental in this care are the notion that healthy newborn infants are physiologically equipped for survival in the environment into which they are born and, secondly, the certainty that, for the building up of a healthy new personality, a firm and comfortable relation between the infant and its mother is essential.

A suitable environment presupposes a mother or mother's substitute whose main concern is the welfare of the baby. She should be one person over a long period, since changing or competing persons make the proper emotional relation difficult. The second vital factor in the environment is food adequate in amount and suitable in quality. Protection from exposure and infection, which is also necessary, has already been discussed.

Introduced into such an environment, the baby has first of all an innate impulse to grow and develop. Growth varies tremendously in its intensity: some well nourished babies weigh 17 or 18 pounds at the age of a year, whereas others weigh 10 pounds more at the same age. Running parallel to the impulse to grow are the senses of hunger, appetite and satiety, which govern much more accurately than any table of calories and ounces the amount of food needed and the frequency of its need. Food forced beyond the requirement indicated by instincts results in no increase in growth.

The impulse toward maturation of the nervous system is as inherent and characteristic as the growth impulse. It can be slowed only by major disasters and probably cannot be hastened by any method of training or feeding. The newborn has not the necessary intellectual equipment to learn by conditioning or teaching, and only begins to develop this faculty during the latter half of the first year. At birth, voluntary movement hardly exists, and years are required for its elaboration and perfection; the lateral tracts of the spinal cord remain only partially myelinated well into the second year. The differentiation between sleeping and waking, apart from the stimulus of hunger, is gradually developed in early infancy.

Emotional needs also tend to mature during infancy, but it appears that for an infantile emotional need to atrophy it must have been amply satisfied at some time. The most urgent infantile emotion seems to be the need for personal attachment to one person. Sucking, mouthing, smelling and feeling all appear to give a sense of emotional relaxation to infants, and many babies become irritable if deprived of them before they are outgrown. It may be that wetting and soiling are similarly satisfying in early infancy. Whether head banging, bedrocking and similar rhythmic motions are to be regarded as normal satisfactions or as evidences of pathologic emotional tensions is dubious, since such habits tend to appear in emotionally tense or defective infants.

Granted these hints regarding a point of view, what are the practical applications? So-called "demand feeding" is one of the most widely discussed issues at present. The notion is to feed the baby when he is hungry and cries for food. Such a schedule is often irregular during the first few days or weeks and is difficult to administer in the average lying-in hospital. Fortunately, most infants seem

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to do well enough on the usual four-hour schedule, with only one or two feedings at breast during each of the first two postnatal days. A few babies, however, seem to be comfortable only on more or irregularly spaced feedings; this is true of both breast-fed and bottle-fed children. In the course of a few weeks on such a schedule, babies tend to cut down on the number and frequency of feedings, so that five feedings a day usually suffice within a few weeks after birth. The physiologic soundness of this method is, of course, attested by the competitive success of mammals in general.

In administering such feedings it should be realized that the reaction of the baby to either overfeeding or underfeeding is much the same, crying being the outstanding symptom. The underfed baby characteristically takes feedings eagerly and hunts for more food when the supply is exhausted, whereas the overfed infant tends to oversleep the next feeding. Hunger in infancy is akin to pain, and pain unrelieved often leads to anxiety and panic. In the majority of cases this mechanism is the foundation of so-called "colic." It is certainly a fact that babies of a few days or weeks cannot be trained to do without a feeding at night or other times. If the desire for food arises, it is in no sense volitional, but is an expression of physiologic need. The sooner this need is met, the faster the baby will be able to gain and store food to allow it to sleep for longer periods, and the less panic and anxiety will have been stimulated.

The introduction of semisolid foods must wait on the development by the infant of the ability to swallow them, and feeding of starches, ability to digest them. An incompletely satisfied appetite helps the baby to want to take new foods, but a really hungry baby expects sucking to be the means to satisfaction and will usually not accept food from a spoon until after at least partially satisfied by breast or bottle; hence, semisolids are usually taken better after the bottle than before.

In the second year appetite is often greatly reduced, many babies in this age group consuming roughly half the food taken a few months previously. At that time a quart of milk a day may well fulfill the caloric needs entirely, and a mixed diet cannot be taken in addition. Drastic cutting of the size of servings — to teaspoonfuls instead of tablespoonfuls and to demitasse instead of eight-ounce cups — will usually keep the child co-operative rather than rebellious at mealtime. Following infections, similar measures may be necessary for a few weeks.

The frequency and character of stools, especially in breast-fed babies, are often far too carefully supervised. Since the stools of the breast-fed infant never become hard and bulky as those of formula-fed babies often do, there is no reason why the infant should have stools at any prescribed interval; certainly, many do well moving their bowels only once or twice a week. On the other hand, some thriving breast-fed babies have many loose, green stools a day. Except for the housekeeping inconvenience, no harm is done, and weaning on this account is not wise.

In bottle-fed babies infrequent stools tend to become hard and may be the cause of rectal fissures, with attendant discomfort and secondary difficulty in bowel training. Proper attention to the formula or the use of a more laxative sugar will usually improve the situation.

Most of the increments of behavior acquired by infants appear by virtue of anatomic and physiologic processes of maturation. Parents know that children sit, stand, walk and talk during stages of natural development. What is not appreciated by many is that babies also give up sucking for their food as they develop — sometimes toward the end of the first year and sometimes not until well into the second year. When the infant is ready to dispense with this method of eating he readily takes to the offered cup and does not need to be "broken from the bottle." Babies so weaned appear to be less likely to suck their thumbs or fingers than those forcibly put on the cup.

Sphincter control is gained by the same process of development. It is acquired slowly in the second year, in most cases, during waking hours and often not until the third or fourth year during sleep. So-called "training" of the infant for stool during the first few months trains the mother or nurse to anticipate the time of the bowel movement and thereby saves laundry, but is of no value. Many babies so "trained," when old enough to control their stools, seem to withhold them purposely when toileted; they are often more difficult to train than those who are first trained when they can understand the process and co-operate. Most babies cannot acquire bladder control in the daytime until well enough developed to announce their needs, and for a long time after this accidents will happen. This point of view is not aimed at relieving the growing organisms of responsibility indefinitely but is oriented toward postponing it until a stage of development appropriate to its assumption has been reached.

School must likewise be regarded as basically a physiologic process of maturation on which the teacher works. Reading readiness tests and the like, given by schools, are a tacit admission by them of the fact. The child placed in the school system at a level beyond his capacity cannot take his responsibility, which for most children is the main aim of education in the long run. A child who must be kept up by extra help and who cannot afford to miss a class or a day at school is usually placed too far ahead in the school system. The temptation to get too far ahead is a strong one, for the child of five or six is so active that the mother is glad to have the school take him off her hands for part of the day at as early an age as possible.

These illustrations are, of course, isolated items from the life history of any child. They are presented in the hope of illustrating the point of view that, given time to mature appropriately before being asked to assume various responsibilities, each child will grow up able to utilize his innate abilities. A baby so handled has the satisfaction of developing new abilities and new aptitudes as a result of his innate endowment, rather than the frustration of having them imposed on him by a system that he neither understands nor desires. Pressure to learn early, constant training and strict discipline may tend to modify these abilities in a downward direction by producing a habit of resistance, frustration and anxiety. Finally, the resilience of the human infant and child must be recognized, for many able adults appear to have been most unwisely handled in childhood.[65–69]

Diagnosis and Management of Seizures

This subject is particularly pertinent for pediatricians, because the younger the animal organism (whether human or subhuman) the greater the susceptibility to seizures, whether these are "spontaneous" or induced by a convulsant drug or fever. Each year the magazine *Epilepsia* reviews approximately two hundred and fifty articles that deal with the subject of convulsions or epilepsy. Yet only two or three articles in a hundred have appeared in a journal devoted to pediatrics. The brevity of the present review emphasizes the apathy of pediatricians toward this important and interesting disease.

Differentiation of the causes of seizures calls for detailed and co-ordinated study of patients with the co-operation of geneticists, obstetricians, pathologists and social therapists and with the aid of laboratory technics, particularly the electroencephalograph. A commendable effort in this direction is the long-term study of 800 epileptic patients at the Harriet Lane Hospital in Baltimore.[70] In 10 per cent of these patients the first convulsion occurred during fever. The prognosis proved to be better when there was a family history of childhood convulsions than if there was none. A report of book length is promised of the neurologic, physiologic and social pathology disclosed by this study.[71] An interesting tabulation of the incidence of convulsions in 1543 children with various pathologic conditions has been made by Crump.[72] For example, convulsions occurred in 7 per cent of patients with extracranial infections, in 55 per cent with meningitis, in 41 per cent with brain tumor, in 39 per cent with encephalitis and in 10 per cent with head and birth injuries. Among 1330 institutionalized patients reviewed by Yannet[73] there were 52 essential (genetic) epileptic patients (3.9 per cent). In addition there were 190 patients (14.2 per cent) with convulsive disorders. In the latter group, cerebral palsy, trauma and infections were most important. Also, the incidence of convulsive disorders was directly related to the severity of the mental defect. A practical and useful discussion of various aspects of epilepsy in childhood is presented by Buchanan.[74]

Fresh contributions to the management of epilepsy have been limited to new anti-seizure drugs. Of these, the preparation of greatest interest to the pediatrician is one that seems to be of specific value in the control of the petit-mal triad. These attacks are frequently repeated transient blackouts, myoclonic jerks or akinetic seizures. Up to now they have resisted drug therapy. Experience has conclusively demonstrated the effectiveness of Tridione (3,5,5-trimethyloxazolidine-2,4-dione) in controlling seizures of the triad.[75, 76] Contrary to the reports of others[77, 78] this drug has been found to precipitate rather than to control grand-mal seizures. It also often causes photophobia, skin rashes or diminution of the white cells, particularly the neutrophils, of the blood. Two deaths from aplastic agranulocytic anemia have been reported.[79, 80] Monthly blood examinations of patients taking this drug should prevent repetition of these disasters.

Demonstration that Tridione seems to have a specific action on the type of seizures associated with an alternate dart and dome formation of the electroencephalogram encourages further laboratory and clinical studies.

Cerebral Palsy

Cerebral palsy is admittedly a frequent and serious condition. Recently, a series of articles suggested treatments with drugs, such as prostigmine[81, 82] and curare, and gave publicity to its educational aspects. Public interest has been excited, and medical advice is being sought by parents whose hopes are high. The urgent need at the moment seems to be not so much information on details as a sound basic philosophy.

By convention, the term "cerebral palsy" is used to describe an abnormality in children who have motor disturbance due to cerebral lesions that have been present from birth. This definition should probably be extended to include cases with onset during the early years of childhood. Obviously, a clear distinction is necessary between cases in which extensive medical study of progressive, active disease may be needed and those in which active disease does not appear to be involved. It is only the latter problems that are discussed here.

The causes of cerebral palsy, as defined above, are, of course, many. There is certainly a group that depends on heredity. Cases of this type seem to be rare and are certainly overemphasized in the literature. A second group depends on vaguely understood prenatal disease or accident to the mother.

Recent work on German measles in the early months of pregnancy has called attention to this phase of the subject, and the occurrence of cerebral palsy in children of mothers who have had bleeding

early in pregnancy supports the theory that various unfavorable events during the early months interfere with normal cerebral development.

Birth injuries are frequent, and it is extremely important to make a clear distinction between birth injury and obstetric error. The former means that the infant was damaged during the extremely complicated mechanical and chemical stresses involved in the process of delivery.[83] There is increasing evidence that a continuous study by obstetricians and their colleagues is throwing light on prenatal asphyxia, the choice of anesthetics, the durability of premature babies, the causes of hemorrhage of the newborn and so forth, as well as on ways to minimize structural trauma during the delivery of full-term babies. All that should be meant by birth injury, then, is that the infant did not withstand the stresses to which it was exposed.

The occurrence of erythroblastosis, with consequent injury to the nervous system, is under constant and productive investigation, and accurate forecasts and preventive measures are available.

Another group of children pass through the perils of birth and the neonatal period and, after a period of normal development, are the victims of some acute encephalopathy, with consequent motor disturbances. Lead poisoning, thrombosis of the cortical veins, subdural hematoma and the various encephalitic processes that occur with measles, whooping cough and the like are examples. Acute and active diseases must be handled by whatever surgical or medical means are available, and no attempt is made to go into this aspect of the problem.

After all evidences of active disease are over, the physician is faced by a task that can be handled in either of two ways. He can take refuge in the hoary and inadequate formula that the nervous system has only two ways of modifying motor patterns. If the anterior-horn cells are damaged, flaccidity will appear, or if any damage above the level of these cells occurs, spasticity will result. There is no validity in this conception, and it should be rejected. On the other hand, the physician can attempt to make a physiologic and psychologic appraisal, which will reveal not only the disability but also the assets of the child, and can then proceed to work out a plan of management.

If this second plan is accepted, the first thing to do is to proceed in an orderly way to determine what the activity of the child is like. From laboratory evidence it is clear that almost complete decerebration may not be inconsistent with life. From this extreme it is entirely possible to go to the most minor and transient disability.

The motor results of cortical injury are to confuse or abolish planned activity. If the basal ganglions are impaired, associated movements are disturbed, with tremor, athetosis and so forth as salient symptoms. In cases of severe diffuse lesions of the whole forebrain, tonic neck reflexes on rotation of the head are frequently seen with consequent extension on the side to which the chin is turned and with contralateral flexion of the arm and leg.[84] Cerebellar lesions, of course, are likely to produce ataxia. It is not difficult to make a rough physiologic appraisal and to compare it with normal behavior at the appropriate age.

Since intelligence is obviously one of the elements in motor control and certainly the controlling factor in effectiveness from the social and economic point of view, an effort should be made to investigate it. Conventional psychometric examination with the result expressed as an intelligence quotient is useful but treacherous. An evaluation by a psychologist who is familiar with handicapped children is better, but even then a single test is less valid than a series at intervals of a year or so.[85]

With the psychologic and physiologic data in hand, it is necessary to consider the effect of the disability in terms of growth and development. At some point it may seem wise to use some of the specialized technics, such as pneumoencephalography and electroencephalography, to obtain a picture of the anatomic and physiologic status of the brain.

Neurosurgical treatment seeks to achieve functional balance by subtraction. If a subtracting technic, such as nerve section, is proposed, it appears reasonable to demand that the family be acquainted with the available physiologic capital from which subtraction is suggested. In the same way, if elaborate and prolonged training procedures are advised, some definite idea of the aim of the procedures should be mapped out.[86] At the moment it seems clear that many patients are being ingeniously treated as children, without any distinct notion of the ultimate results in terms of adult competitive activities.

The numerous organizations that are dealing with the disabilities of children will be wise if they face resolutely the disconcerting fact that the average child suffering from cerebral palsy comes to adult life unprepared for the competitive world that may be too much for him. The test of successful guidance during childhood comes at adolescence or in early adult life. So far, the results have not been good.

Orthopedic Surgery

A new method of treatment of congenital clubfoot was introduced by Denis Browne in 1933, in which the feet were strapped to metal plates connected by a cross bar. Correction was obtained by forceful kicking on the part of the infant. This procedure was reintroduced and modified by Thomson of Toronto in 1942 and has greatly facilitated the early correction of congenital clubfeet.[87] It has proved a valuable adjunct to the usual methods of correction by manipulation and plaster casts. Emphasis should be placed on the institution of early treatment, since this technic is particularly applicable to the newborn infant, and the earlier treatment is instituted, the better the end-result.

Eosinophilic granulomatous lesions of bone have recently been described by Lichtenstein and Jaffe[88] and by Green and Farber[89] and an attempt has been made to place these lesions in their proper category among bone dyscrasias. The former authors believed that they were describing a new clinical and pathological entity, whereas the latter indicated that the lesion was related to the lipoid diseases of bone, variously considered under the names of Hand–Schüller–Christian and Letterer–Siwe diseases. Regardless of the true category, the term "eosinophilic granuloma" is a useful one to bear in mind when cyst-like lesions of bone, many of which were formerly thought to be malignant and were frequently diagnosed as multiple myelomas, are being considered.

The early diagnosis and more rational treatment of slipped femoral epiphysis have recently been emphasized in an effort to prevent the severe crippling that ensues when the condition is neglected.[90, 91] Probably no lesion of developing bone is more serious in end-result than a bilateral slipped femoral epiphysis, which produces degenerative changes in both hip joints. Any child between the ages of nine and fifteen years, particularly if obese, who complains of pain in the hip, knee or anterior thigh should be carefully evaluated, the possibility of a slipped femoral epiphysis being always borne in mind, and early x-ray films of both hip joints obtained. Early diagnosis is essential if a normal hip joint is to be maintained.

Progress in the orthopedic management of poliomyelitis centers around the introduction of the Kenny method of physiotherapy and its supposed conflict with accepted methods of treatment.[92–94] Since varying physiotherapy technics are usually expressions of temperament and background rather than new discoveries, the introduction of a new variation would have excited little comment, were it not for the crusading fervor of its founder and the deliberate and belligerent attack on the older and less dramatic procedures in vogue. The Kenny method emphasized the value of early mobilization of paralyzed extremities by active exercises, as well as the dangers inherent in rigid and prolonged immobilization. All of this is desirable. The rest of the method might be dismissed as redundant, were it not for unhealthy press, radio and cinema publicity, which tends to overemphasize the value of this form of physiotherapy in the convalescent management of poliomyelitis.

Acute hematogenous osteomyelitis is essentially a disease of children. Treatment has changed radically with the introduction of penicillin.[95, 96] Therapy in children under two years of age has been conservative, but in older children, treatment in the past was mainly surgical, with incision and drainage and packing of wounds. Chronicity and prolonged invalidism usually resulted. The present management of acute osteomyelitis is to use penicillin as soon as possible after onset and in large doses. The degree of bone damage is directly proportional to the time elapsing between onset and drug therapy. Of great importance is education of pediatricians to the value of early diagnosis and early medical therapy. Frequent examination of the local lesion, however, is necessary, and the indications for surgery should be well outlined. These include abscess formation and persistent and increasing pain and swelling of the affected part, in spite of adequate dosage of the drug. It is highly desirable to take a blood culture on the child before therapy is instituted, since in this manner the organism can frequently be identified and its sensitivity to penicillin determined. Penicillin therapy should be continued for at least three weeks, or longer if indicated. Surgery should always be minimal and directed toward a specific objective, such as evacuating an abscess or decompressing a bone lesion. Extensive bone stripping and packing are obsolete. Closure of the wound around rubber tubes or cannulas and instillation of penicillin solutions postoperatively lead to early healing and minimal scarring and dysfunction, and in most cases acute osteomyelitis heals without the development of chronic osteomyelitis. This type of management of acute hematogenous osteomyelitis represents a drastic departure from the older methods rather than a modification of technics.

Acute osteomyelitis in children was formerly invariably followed by prolonged suppuration and chronic bone infection. The management of chronic osteomyelitis has altered radically with the introduction of penicillin. At present, it is recognized that necrotic material must be removed surgically. Exploration of draining sinuses and sequestrectomy are still fundamental, but with parenteral drug therapy and direct instillation of penicillin into the wound through tubes, early secondary closure is possible and prolonged suppuration and spread of infection to adjacent bone may be avoided.[97]

New technics have been introduced in the treatment of deformities due to unequal length of the lower extremities. Surgical procedures for lengthening shortened extremities have largely been replaced by selective ablation of the epiphyses in the longer extremity. This procedure, usually termed "epiphyseal arrest," is performed during the period of active growth, and the "timing" of the operation is determined by reference to tables that give average growth expectancy for the epiphyses at various ages. Recent studies on the effects of irradiation on epiphyseal growth may result in quantitative reduction in growth by selective roentgenotherapy of epiphyses at various ages, without recourse to surgery. This procedure is still highly experimental and dangerous, and so far not sufficiently perfected to be used clinically, but offers a promising field for the future.[98]

In all methods of equalizing leg length, careful and accurate measurements at various intervals are essential. A useful procedure of accurately measuring the bones of the lower extremities has recently been introduced.[99] It is essential that physicians in pediatrics and general practice appreciate the possibility of equalizing leg lengths and thus of preventing serious deformities in adult life. Children with lower extremities of unequal length should be referred for orthopedic treatment long enough before the time of natural closure of the epiphyses so that equalization by arrest is possible.

Gastrointestinal Disorders

Acute Diarrheal Disease

Progress in the understanding of the causes of diarrheal disease has received considerable impetus from recent work on the isolation of viruses from patients with diarrhea.[100–103] These studies are particularly stimulating because the search for a causative organism in the form of bacteria has frequently been disappointing. In spite of the tremendous reduction in the incidence of diarrhea there has continued to be frequent epidemic and endemic diarrhea whose cause remains obscure.

The use of the gamma-globulin fraction of human serum had no influence on the course or mortality of infants suffering from epidemic diarrhea of the newborn.[104] It will be of interest to watch the result of further studies along these lines, provided that viruses are found as a frequent cause of diarrhea.

Great progress has been made in the past decade in the treatment of the effects of diarrhea by repair solutions calculated to correct dehydration and acidosis. The importance of establishing renal function as an initial phase in the correction of the disturbed serum electrolyte pattern has been reemphasized in a recent report.[105] It is opportune that this should be stressed in the light of current developments in elaboration of repair solutions. It should never be forgotten that the most sophisticated repair solution cannot be depended on to replace the wisdom of an alert and capable kidney in restoration of the normal electrolyte pattern.

Up to the present attention has been focused mainly on the major deficits of sodium and chloride resulting from diarrhea. It has long been recognized that other deficits existed, not only in the blood plasma but also in the intracellar electrolyte system.[106, 107] Particular interest now centers on the deficit of potassium. Further information regarding the loss of potassium from the body during diarrhea is provided by recent contributions.[108] That potassium may be provided in a satisfactory solution and this deficit safely corrected has also been reported.[109, 110] Details for the preparation and use of this repair solution are given in these reports. In the group of patients receiving this treatment, the mortality was considerably reduced, and some of the symptoms were apparently relieved.

It is difficult to determine the symptoms that can be attributed to a deficit of potassium. Symptoms expected from low levels of serum potassium are those secondary to impaired functioning of striated muscle — for example, diaphragmatic and myocardial paralysis.[111] Considerable definition of all symptoms is still required. Furthermore, mortality alone may not suffice for the complete evaluation of any beneficial effects of the addition of potassium to a repair solution. This has been illustrated by the recent experience of attempting to evaluate the usefulness of amino acid-containing solutions to replace the nitrogen deficit that occurs in acute diarrhea. The validity of repair solutions to provide materials that correct all deficits occurring in acute diarrhea will be most adequately appraised when the results in patients suffering from all types of diarrhea can be evaluated, in contrast to the results in a single epidemic of diarrhea.

A note of warning is pertinent regarding certain dangers involved in the parenteral administration of solutions containing potassium ion. In patients suffering from dehydration and acidosis, the level of potassium in the serum may already be somewhat elevated.[110] If further potassium is supplied by a repair solution either before renal regulatory mechanisms are restored or too rapidly, the level of potassium in the serum may reach a toxic level — an accident that actually occurred in an infant under such therapy.[112] This serves to re-emphasize the basic consideration that the restoration of renal function with sodium chloride and glucose solutions should be the initial phase of therapy.

Patients in a severe state of disturbed serum electrolyte pattern associated with either adrenocortical insufficiency or renal failure might well have their fate imperiled by potassium-containing solutions if the condition were not suspected. Such patients are regularly encountered.[113, 114] In this clinic we have already had a nearly disastrous result from the administration of a potassium-containing repair solution to a child presumably suffering from adrenocortical insufficiency even though urine flow had been first re-established with glucose and sodium chloride solutions.

It now appears that sulfadiazine is as useful as any of the more specialized sulfonamides, such as succinylsulfathiazole and sulfaguanidine, in the treatment of the acute bacterial dysenteries in infants and children.[115]

Oral streptomycin has been advocated and used with some success in the treatment of infectious diarrhea due to specific sensitive enteric organisms.[116]

Fibrosis of the Pancreas

Clinical and pathological reports concerning this disease continue to appear with regularity. The cause of the disorder remains obscure. The current

theories are listed in a recent review.[117] One report presents questionable evidence and analysis implicating heredity as the basis of the disorder.[118] The wide variations of clinical appearances of this disorder are now apparent. These range from the association with meconium ileus in the newborn to the chance finding of patients five to nine years of age in relatively sound states of nutrition and with minimal pulmonary signs.

In the original reports most of the infants died before two years of age. The present therapeutic efforts appear to be increasing the survival period of these patients. Such treatment comprises provision of an adequate diet, substitution therapy in the form of pancreatin and attack on the pulmonary lesions so far as superimposed infection is concerned. In this connection Farber[119] has emphasized the presence of a basic lesion in the lungs dependent on the production of abnormal secretions by the mucous glands. Some exception has been taken to this view in a recent report by Wigglesworth,[117] but this point is of paramount importance in a consideration of therapy for pulmonary lesions. If altered secretions form the basis of the disease in the lungs, little can be expected from the effort aimed at eradication of superimposed infection. On the other hand, if the infection that is frequently present constitutes a significant portion of the pathologic process in the lungs, it is imperative to focus therapeutic effort toward its eradication, and the results to be expected might be more favorable. The use of sulfonamides orally and of penicillin intramuscularly has met with only partial success in the control of infection. Recently, the use of penicillin and sulfonamides in the form of aerosol inhalation therapy has provided a new approach to the treatment of intrapulmonary infections.[120, 121] Experience reported recently indicates that the pulmonary lesion can be considerably influenced by this sort of treatment.[122] A number of patients have shown considerable clearing of the pulmonary infiltration, with corresponding improvement in their clinical well being, as revealed by a gain in weight and subsidence of cough and fever. It is quite clear, however, that the entire pulmonary lesion is not obliterated, since much of the infiltration remains and some wheezing or cough may persist. Furthermore, the patients are still extremely susceptible to recurrences of pulmonary infection.

Complete descriptions of the roentgenologic features of this disease have appeared.[123] In Neuhauser's[124] paper particular attention has been devoted to the roentgenologic characteristics of meconium ileus, with the elucidation of certain helpful diagnostic signs.

There is a genuine need for a simpler means of establishing the diagnosis of fibrosis of the pancreas once it is suspected. A new approach to this problem utilizes a rise in amino acid level in the blood following a test meal.[125] In patients with fibrosis of the pancreas who have no enzymes in the duodenum, there is little fluctuation of the postprandial amino acid level. Other chronic disturbances of intestinal absorption, such as celiac disease, in which there are normal enzymes in the duodenum, show a significant and comparatively high rise of amino acid level in the blood after the test meal.

Celiac Disease

The reports of the successful treatment of adult sprue with folic acid naturally arouse curiosity concerning similar effects in celiac disease of childhood.[126] In this clinic we have treated 8 well established cases of this disorder with folic acid without any effects on the steatorrhea or any of the other clinical or laboratory features of the disease.[127] Two patients with the diagnosis of celiac disease were treated by English physicians with folic acid, and benefit was reported.[128, 129]

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CASE 33241

PRESENTATION OF CASE

A sixty-three-year-old man was admitted to the hospital because of heartburn and abdominal pain.

He complained of heartburn for the previous two years with a dull, constant occasionally sharp pain across the upper abdomen that had extended into the back, especially in the right infrascapular region, in the preceding two months. "Pills" had no effect on the pain, but he felt better when lying on the left side. Three months prior to admission a gastrointestinal series at an outside hospital showed no evidence of ulcer but did show a diaphragmatic hernia. Immediately following the x-ray studies the patient ate a heavy meal, with subsequent repeated vomiting for one day. About that time he noticed slight constipation and subsequently had two black stools. About a month and a half before admission painful ankle edema and occasional shoulder, elbow and wrist pains began. He also noted increasing weakness and a weight loss of 25 pounds in the three months prior to admission.

Physical examination revealed a well developed man showing evidence of recent weight loss. A Grade I apical systolic murmur was noted, with occasional extrasystoles but no enlargement of the heart. The lungs were clear. There was slight tenderness to palpation just beneath the right costal margin, but the liver and spleen were not felt. A few observers felt a deep but indefinite palpable mass in the right upper quadrant. There was a ++ to +++ pitting edema of the lower legs, more so on the right.

The temperature was 100°F., the pulse 96, and the respirations 20. The blood pressure was 130 systolic, 80 diastolic.

Examination of the blood showed a hemoglobin of 13 gm. and a white-cell count of 16,500, with 71 per cent neutrophils. The urine was normal, as were the stools. The serum protein was 6.2 gm. per 100 cc., with an albumin-globulin ratio of 0.9. The nonprotein nitrogen, prothrombin time, amylase and fasting blood sugar were within normal limits. A blood Hinton test was negative. A Graham test did not reveal a gall-bladder shadow. An intravenous pyelogram was essentially normal. There were old compression deformities of the fourth and fifth lumbar vertebras and moderate degenerative changes of the spine. An x-ray film of the chest revealed moderate scoliosis of the thoracic spine, with a convexity to the right, and calcification of the wall of the aortic arch. A barium enema disclosed no evidence of intrinsic disease. The gastrointestinal series revealed a small hiatus hernia that reduced itself while the patient was in the upright position. No other abnormality was found.

On the fourth hospital day following an enema the patient began to perspire and fainted. He stated that he had passed a large black stool, but he was on iron therapy and the feces were not saved for examination. During the night of the fourth hospital day he had a severe attack of epigastric pain, which was relieved by firm rubbing of the upper abdomen. The following afternoon, ten minutes after finishing lunch, he developed a boring pain running from front to back in the epigastrium without nausea or vomiting. Sitting up did not relieve the pain. Another Graham test showed no filling of the gall bladder. Duodenal drainage on the seventh hospital day revealed clear, yellow fluid but no sign of blood. Examination of the material disclosed numerous bile-stained white cells and crystals. A cephalin-flocculation test was +++, both in twenty-four and in forty-eight hours. The serum amylase determination was 29 units, the blood calcium 7.2 mg. and the phosphorus 3.7 mg. per 100 cc., and the phosphatase was 4.5 units. An electrocardiogram was normal. In a bromsulfalein test the five-minute sample was too dark to read, and in forty-five minutes there was 22 per cent retention of the dye. Subsequent to the duodenal drainage the patient developed a fever, the temperature rising to 101°F. each day, and the pain was rather severer than at the time of entry.

At the end of two weeks the temperature became normal, and on the seventeenth hospital day a laparotomy was performed. At operation no abnormalities could be discovered on palpation or inspection of the abdominal viscera. Because of the positive Graham test on two occasions and the pus and crystals in the duodenal drainage, the gall bladder was removed from above downward without incident. The common duct, which was then opened and explored, contained clear bile, and probes passed readily into the duodenum. A liver biopsy was also performed.

On the fourth postoperative day the patient complained of upper abdominal pain similar to that before operation. The next day he complained of numbness and paresthesias in the hands, and neurologic examination revealed diminished sensation to pinprick in the distal phalanges of the left hand and over the lateral aspect of the right lower leg and foot. On the following morning the patient awoke complaining bitterly of pain and inability to

move the left foot. Physical examination showed no change in color or temperature of the foot. There was anesthesia over the entire leg below the knee except for a 5-cm. band along the medial aspect.

Differential Diagnosis

Dr. Wyman Richardson: I might begin by saying that I have arrived at a fantastic conclusion, and that I apologize ahead of time for it.

"A few observers felt a deep but indefinite palpable mass in the right upper quadrant." I think that one must forget about this mass; with only a few observers feeling a deep but indefinite mass it remains deeply obscure and quite indefinite to me.

This is a case in which a blood smear would have been helpful in the differential diagnosis. I shall point out here that a leukocytosis of this extent, with only 70 per cent neutrophils, is strong evidence against pyogenic infection as the cause of the symptoms, and also against bacterial endocarditis alone as the cause of the symptoms. The blood picture suggests fairly recent and acute blood loss or infarction; or if there were evidence of red-cell regeneration it would suggest the possibility of bone-marrow encroachment. We do not know whether there was red-cell regeneration or not. There are other kinds of infection that might cause this type of blood picture, but without further data, I do not believe that one need consider them. This picture is compatible with loss of blood into a cavity or with extravasated blood.

I assume that a good many stool examinations for occult blood were done and were negative.

I wonder why the albumin and globulin were not reported in grams, rather than the albumin-globulin ratio. It is easier for me if the report is in grams, my mathematics not being too good. In this case I should say that there was about as much albumin as globulin.

Perhaps we should see the x-ray films. I am anxious to know if there is any evidence suggesting tumor involving bone in either the lumbar or the cervical spine. I do not believe that films of the cervical spine were taken, however.

Dr. Toufic Kalil: The only thing that I can see is the hiatus hernia that was described as being readily reducible on standing.

Dr. Richardson: I am uncertain whether the hiatus hernia accounted for this man's pain. Do you see the deep and indefinite mass in the right upper quadrant? Nothing was observed in that area at operation.

Dr. Kalil: No.

Dr. Richardson: Is this an old fracture of the spine?

Dr. Kalil: All the bones are decalcified. Without a lateral view of the lumbar spine, one cannot tell much about it. There is no localized destruction. The intravenous pyelogram is normal.

Dr. Richardson: The question is, Did this man faint because he had a sudden hemorrhage? I should say that a man who fainted suddenly from hemorrhage would not immediately pass a black stool. To account for the fainting, he would have to have had a massive hemorrhage, and if he immediately passed a stool it would definitely have been bloody. What else could happen to a man who had an enema? I suppose that many things could occur. Patients may feel faint without any pathologic reason. I think that this episode may have been significant, although I am not quite sure of what. One could have perforation of the bowel following an enema, but there was no evidence of peritonitis following it. For the moment I shall say that perhaps something occurred when the enema was given. It may turn out to be of some importance, but it was probably not a sudden acute hemorrhage. No guaiac-positive stools were reported following this incident.

The record does not state whether the crystals found in the duodenal drainage were cholesterol or bilirubin. I do not rely too much on the cephalin-flocculation test. I wonder if it was associated with the slight increase in globulin. The serum amylase was 29 units per 100 cc. I believe that is normal. Do you agree, Dr. Jones?

Dr. Chester M. Jones: Yes.

Dr. Richardson: The blood calcium was somewhat low, as was the serum albumin. I do not know whether that is significant or not. The bones were somewhat decalcified. Most of the blood chemical findings were normal. The phosphorus was slightly high but, I should think, within normal limits.

It is not stated whether the bromsulfalein test was done with a 2-mg. or a 5-mg. dose; presumably, it was 5 mg. I should say that there was slight increase in bromsulfalein retention but within a range that was not sufficiently characteristic to lead to any specific diagnosis. At least, I shall say that it was not severe enough to make it certain that there was any considerable degree of hepatic failure.

Evidently, it was considered quite possible that this man had gallstones. I cannot imagine that the surgeon did not open the gall bladder, and I gather that no stones were found, although nothing is said. I believe that the gall bladder was removed more or less on theoretical grounds.

The record does not mention peripheral arterial pulsation, which I think is extremely important in this case.

One of the things that helps a great deal in these discussions is the knowledge that the patient died. I do not know whether this patient died or whether he got well. I might say that I am doubtful if Dr. Castleman can make a diagnosis on the basis of a small liver biopsy, and I suspect that he had more material to examine than a small piece of liver. I assume that the patient's subsequent course was so characteristic as to give the diagnosis away and

perhaps spoil the fun of these exercises — that is, fun for you but not for me. I thought that, instead of going round and round this diagnostic circle, I should take one symptom and see what I could do with it.

The peculiar complication of this case is the peripheral neuritis. I do not believe that it was due to nutritional deficiency; I say so because of the onset. The pain, which was sudden in its development, was patchy and not symmetrical, and hardly compatible with a diagnosis of nutritional deficiency.

Was the prothrombin time normal?

DR. JONES: Yes.

DR. RICHARDSON: What about infectious polyneuritis? I have never seen a patient with this disease who reacted in this fashion. Many of the facial nerves are first involved, and sometimes these are the only nerves affected. There are other types of infectious polyneuritis, but I do not believe that there is much evidence for obscure diseases.

Did this man have active tabes, with everyone thrown off the track? The pain of tabes is not of this type. Usually, it involves the lower limbs, with, in the early stages, no definite evidence of impaired sensation.

What about metastases to bone or malignant tumor in the region of the sacral or brachial plexuses? This has not been ruled out and remains a possibility, although there was no x-ray evidence of bone metastases and no evidence of tumor on abdominal exploration.

A final possibility is some other type of central-nervous-system infection or neoplastic invasion. There is no report of a lumbar puncture. Nothing in the blood picture supports a diagnosis of sepsis, although the patient was running a mild fever.

Could this neuritis have been arterial in origin? I do not understand why, when an artery becomes plugged, neuritic symptoms appear. I do not want to go more deeply into this question.

Periarteritis nodosa is a diffuse disease associated with neuritis, fever and abdominal pain, and that diagnosis must be considered in this case. Again, the onset of the neuritis was peculiar for periarteritis nodosa. The type of abdominal pain due to small mesenteric thrombosis or infarctions is usually referred to the midline and is more generalized. Although one should bear in mind the possibility of periarteritis nodosa, I do not believe that in this case one can make such a clear-cut diagnosis. I come down to the fantastic theory that this man had arterial disease, which was perhaps localized in the region of the abdominal aorta, at the level of the pancreas. All this midepigastric boring pain going through to the back is quite typical of pancreatic pain, or pain in that area. I suspect that the patient had an ulcerating lesion in the region of the pancreas, with erosion into the aorta and actual

FIGURE 1.

dissection of the aorta up and down. He may have had a moderate degree of cirrhosis of the liver, but I do not believe that it was significant. If this is not a fantastic diagnosis, I have never heard of one.

DR. WALTER BAUER: I believe that you should not have lost the diagnosis of periarteritis nodosa.

DR. RICHARDSON: I was going to flip a coin but then decided on a flat-footed diagnosis.

DR. BAUER: The white-cell count was 16,000, which is suggestive, and the other symptoms are readily explained on the basis of periarteritis nodosa. It certainly accounts for the recurring attacks of abdominal pain. I should make a diagnosis of periarteritis nodosa.

DR. RICHARDSON: I accept that as a possible diagnosis. I doubt if the patient had it. Does anyone else want to suggest an alternative diagnosis?

A PHYSICIAN: How about acute porphyria? Would it fit in with the findings in this case?

DR. RICHARDSON: I had not thought of porphyria as a disease. I considered lead colic and neuritis, which I did not think probable. I am not able to rule out acute porphyria.

DR. JONES: We had a case of porphyria six weeks ago with repeated attacks of severe abdominal pain, and I think that that condition should be included at least in the differential diagnosis.

DR. BENJAMIN CASTLEMAN: Will you tell us about the operation, Dr. Taylor?

DR. GRANTLEY W. TAYLOR: I should apologize for operating at all. The patient had lost a good deal of weight, had become progressively weak and had a somewhat elevated white-cell count and intermittent fever. The most incapacitating symptom was the severe pain that went through to the back. The only evidence that we could tie up with that as possibly being helpful was the character of the duodenal drainage and the two positive Graham tests. There was no jaundice, and we thought that all these symptoms might have occurred on the basis of carcinoma involving the body of the pancreas or that the patient had disease related to the gall bladder and common duct. I must say that it was a completely negative exploration. The hiatus hernia did not seem to account in any way for the symptomatology. Then the problem was what to do — whether to let him alone, sew him up or take out the gall bladder on the ground that the symptoms were due to gall-bladder disease that was not obvious from external examination of the organs. We also explored the common duct on the suspicion that cholangitis was present, but the bile duct proved to be perfectly normal. We removed the gall bladder and took a liver biopsy, thinking that we might turn up with something.

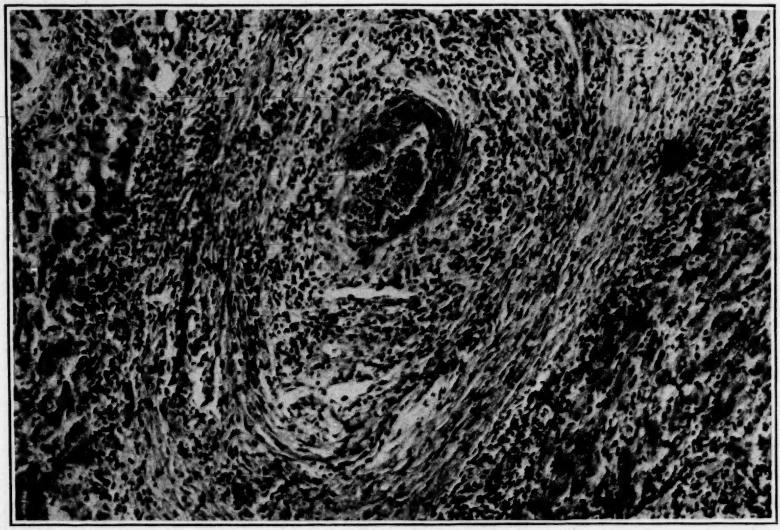

FIGURE 2.

DR. RICHARDSON: Regarding the nonfilling gall bladder, I meant to suggest that it might have been due to a poorly functioning liver. It will be recalled that there was some degree of dye retention.

CLINICAL DIAGNOSIS

Carcinoma of body of pancreas?

DR. RICHARDSON'S DIAGNOSIS

Ulcerating lesion, pancreatic region, causing aortic erosion and dissection.

ANATOMICAL DIAGNOSES

Periarteritis nodosa involving gall bladder and liver.

Infarcts of gall bladder.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The gall bladder that we received looked fairly normal except for a few small, dark, hemorrhagic, questionably ulcerated areas on the mucosa. The rest of the mucosa was smooth, shining and velvety. On microscopical examination we found in the wall of the gall bladder many arteries whose walls were necrotic and heavily infiltrated with polymorphonuclear leukocytes and lymphocytes. The findings were quite characteristic of periarteritis nodosa. Elastic-tissue preparations showed marked destruction of the elastica. Some of the vessels were thrombosed and accounted for the focal mucosal ulcerations, which were really focal infarctions (Fig. 1). We found the same process on liver biopsy — extensive necrosis of the small arteries, with thrombosis. In places organization of the thrombi with recanalization had occurred (Fig. 2).

This man is still on the ward, Dr. Richardson, and we do not know what the final situation is. Can you tell us how he is, Dr. Dahl?

DR. LEWIS K. DAHL: He is going downhill rapidly.

DR. RICHARDSON: Did he ever have any eosinophilia?

DR. DAHL: No.

DR. RICHARDSON: Had he ever been given any sulfonamides?

DR. DAHL: We could not obtain any history of sulfonamide administration. The patient does not speak English very well, but he gave no history of taking tablets that suggested the sulfonamides.

DR. RICHARDSON: What was the anatomic cause of the boring epigastric pain?

DR. CASTLEMAN: I believe that the infarction of the gall bladder could have caused the pain.

CASE 33242

PRESENTATION OF CASE

A seven-month-old male infant was admitted to the hospital because of a mass in the right abdomen.

The child was born after an uneventful pregnancy and weighed 8 pounds, 12 ounces. Development was normal, and the day before admission his mother first noticed a mass in his right abdomen.

Physical examination showed an overnourished infant in no distress. There was a firm, rounded fairly smooth, nontender mass occupying the right half of the abdominal cavity and extending from beneath the right costal margin to just below the level of the right iliac crest. The rest of the examination was negative.

Examination of the blood revealed a white-cell count of 19,600, with 49 per cent neutrophils, 45 per cent small lymphocytes, 4 per cent monocytes and 2 per cent eosinophils. Urine and stool examinations were negative. An intravenous pyelogram revealed an unusually large right kidney, which was smooth. The left was obscured by gas but appeared within normal limits. The right kidney produced bulging of the abdominal wall laterally. Excretion of dye was prompt in both kidneys. The urinary passages on the left were poorly seen but showed no gross abnormality. On the right there was gross crowding of the calyxes in the upper half of the kidney upward and of the lowermost calyx downward and inward. There was no evidence of gross invasion of the calyxes or pelvis.

On the fifth hospital day an exploratory laparotomy was performed.

DIFFERENTIAL DIAGNOSIS

DR. LEO BURGIN: This brief history leads one at once to the problem of the etiology and nature of an abdominal mass in a seven-month-old infant who had previously been well.

The x-ray report of an enlarged kidney producing bulging of the abdominal wall suggests that the mass was at least retroperitoneal. This simplifies matters somewhat in that a host of abdominal possibilities, such as congenital cysts, reduplications, hepatoma, abdominal lymphoma and Hodgkin's disease, may be excluded.

Since we have decided that the tumor mass was retroperitoneal, our next consideration is whether or not it was malignant and finally, what was its nature. From a practical standpoint one should follow Farber's* generalization, "Every solid mass in an infant or child should be regarded as a malignant tumor and removed in its entirety for histological examination and determination of its exact nature." Presumably, this was carried out in the present case.

For purposes of discussion we should rule out a "benign" condition such as cystic disease of the kidney — multiple or single. There is no evidence of abnormal kidney function such as albuminuria or hematuria. Of course, with small cysts there may be sufficient normal renal tissue for an infant of this age. With a mass such as that described, how-

*Farber, S. Malignant tumors in early life. In *Textbook of Pediatrics.* Fourth edition. 1320 pp. Philadelphia: W. B. Saunders Company, 1945. Pp. 315-323.

ever, one would expect some abnormal urinary findings if it had been due to cystic disease. One would also expect more distortion of the renal pelvis, possibly with an x-ray appearance consistent with the so-called "spider pelvis" deformity. The latter picture is by no means diagnostic of this condition, which has been reported in cases of embryoma of the kidney. Cystic disease is generally bilateral — in 98 per cent of cases, according to some authors.

retroperitoneal space and about the adrenal glands. There is no characteristic picture other than the presence of an abdominal mass. One may encounter nonspecific complaints of fever, anorexia, bowel disturbances and so forth. If there has been metastasis to bone, and this is common with neuroblastoma, there may be pain in the extremities.

Embryoma of the kidney is an encapsulated tumor arising within the kidney. The tumor is firm,

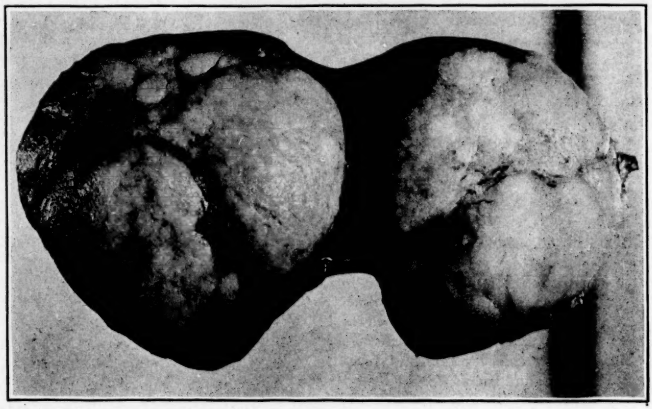

FIGURE 1.

The prompt excretion of dye by both kidneys is further evidence against such a diagnosis.

With much of the previous evidence one can rule out hydronephrosis due to obstructive uropathy resulting from congenital malformations. Inflammatory processes may likewise be excluded. We might, in passing, mention such benign tumors as lipoma, fibroma and myoma only to note that these are extremely rare and not likely to produce the picture described here.

We are then led to consider at once some of the malignant tumors of this region. In children under two or three years of age the commonest tumors occurring in the renal region are the embryoma of the kidney (Wilms's tumor, or mixed tumor of the kidney) and tumors of the neuroblastoma series. One might also include occasional mixed tumors arising from tissues outside the kidney but in the retroperitoneal spaces. One should perhaps include hypernephroma. There seems to be some question whether such a tumor ever occurs in infancy. I do not believe that we need consider it in this case.

The neuroblastoma may arise within the adrenal medulla or from sympathetic nerve tissue in the smooth and rounded in outline. It often extends to the midline and to the iliac crest. Since such tumors arise within the kidney, we expect to find distortion of the renal pelvis by x-ray examination. Occasionally, the deformity may be confused with that produced by cystic disease, as I have indicated above. The tumor is usually unilateral. Neuroblastoma occasionally arises within the kidney from inclusions of adrenal medullary tissue present there and consequently gives a picture indistinguishable grossly from embryoma.

The sudden appearance of the tumor one day before admission may be difficult to reconcile with the physical examination on admission. The life history of these tumors, however, includes such phenomena; generally, massive hemorrhage into a tumor that is starting to grow rapidly may make the tumor noticeable in cases in which examination a few days previously has revealed no mass. The elevated white-cell count may have been in response to the hemorrhage or necrosis, or both, that may have been taking place.

The sudden appearance of a firm, smooth tumor mass involving the kidney, with x-ray evidence of a

distorted pelvis but good function, and a normal urine in an otherwise normal infant suggests the presence of a mixed tumor of the right kidney. I believe that this infant had a Wilms's tumor.

DR. STANLEY WYMAN: These films show the enlarged right kidney pressing on the lateral wall of the abdomen. The upper and lower calyxes in this film are crowded upward and downward respectively, but no definite intrinsic involvement of the walls or the pelvis can be determined. No evidence of disease can be seen in the bones of the spine or chest.

CLINICAL DIAGNOSIS

Wilms's tumor of kidney.

DR. BURGIN'S DIAGNOSIS

Wilms's tumor of kidney.

ANATOMICAL DIAGNOSIS

Wilms's tumor of kidney.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: At operation Dr. Robert R. Linton found a large tumor of the kidney, which he removed without difficulty. It was not adherent to any of the surrounding structures and had not broken through the capsule of the kidney. The tumor measured about 8 cm. in diameter and had replaced most of the renal parenchyma, leaving only a narrow rim of cortex (Fig. 1). It appeared to be completely surrounded by a fibrous capsule and did not invade the pelvis or calyxes. Microscopically, the tumor was composed of both tubular and spindle-cell elements, which are the characteristic findings in a Wilms's tumor or what is often called "embryonal adenosarcoma." A few regional lymph nodes removed with the kidney showed only hyperplasia.

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BLUE SHIELD ADVANCES

On June 1, 1947, Blue Shield took an important step forward. On that date its present program of surgical and obstetric benefits in the hospital was extended to include medical (nonsurgical) benefits in the hospital and surgical and obstetric benefits outside the hospital. At the same time, a new schedule of fees for services rendered to holders of Blue Shield policies became effective.

Undoubtedly the latter will receive the utmost attention and a certain amount of criticism, particularly from those participating physicians who are surgeons. The schedule is the result of careful study and of many time-consuming meetings of the committees appointed to prepare it. The committees were composed of specialists in their various fields, who agreed that Blue Shield fees should not be based on the customary value of a specialist's services but on the ability of individuals and families in the under-income group to pay for such services. Much consideration was given to the relative difficulty of procedures not only within the specialties but also between the specialties, with the result that procedures of comparable difficulty in, for example, ophthalmology and urology were assigned similar fees so far as it was possible to do so. At first glance the level of fees may seem low, but when it is remembered that they apply to low-income patients, many of whom were previously medically indigent and to patients who were formerly poor credit risks, their adequacy is more easily visualized. It should also be recognized that the schedule applies on a state-wide basis.

With nearly 600,000 persons covered, Blue Shield is now the second largest and one of the most prosperous medical-care plans in the Nation, and much of its success is attributable to the fact that physician participation, originally in the neighborhood of 50 per cent, has rapidly climbed to its present level of over 90 per cent. The Blue Shield Board of Directors, made up of one third physicians and two thirds lay persons, is elected by the Executive Committee of the Council of the Massachusetts Medical Society, and before any rules or regulations affecting medical matters can be implemented they must be approved by the Executive Committee. Furthermore, in each district medical society there is a Blue Shield Professional Service Committee, through which the practicing physician can make his voice heard.

The ultimate success of Blue Shield rests primarily on the degree to which the medical profession, collectively and individually, participates. Because of the overwhelming importance of this venture, every physician who is interested in maintaining the voluntary approach to the problem of the costs of medical care and who is not yet a participant should request that he be supplied with an application form. Such letters should be addressed to Massachusetts Medical Service, 38 Chauncy Street, Boston 11.

THE EFFECT OF DI-ISOPROPYL FLUOROPHOSPHATE ON PATIENTS WITH MYASTHENIA GRAVIS

MUSCULAR fatigue, characteristic of the weakness in patients with myasthenia gravis, is thought to result from an insufficiency of acetylcholine at the myoneural junction. This insufficiency may be due to a decreased formation of acetylcholine (faulty metabolism), to an increased cholinesterase activity destroying the acetylcholine more rapidly than under normal conditions or to a decreased activity of acetylcholine itself, possibly caused by the presence of an antagonistic curare-like substance. There is no unequivocal evidence at present to support a view that any one of these postulates accounts for the chief symptom of myasthenia gravis, but it is agreed by all investigators that the acetylcholine-cholinesterase balance is disturbed at the myoneural junction in this disease. It has been shown, moreover, that cholinesterase is inhibited by neostigmine or physostigmine, the two drugs ordinarily used in the treatment of this disease. Because of the ease with which it is tolerated by patients, neostigmine has replaced physostigmine.

Although neostigmine is reasonably efficient, other anticholinesterase agents are now under investigation. Recently, di-isopropyl fluorophosphate (DFP), a compound unrelated chemically to neostigmine, was found to produce inhibition of serum, red-cell, muscle and brain cholinesterase in animals. The results of treating myasthenic patients with this drug have now been reported by Comroe and his associates,[1] working at the University of Pennsylvania Medical School and the Medical Research Laboratory, Chemical Warfare Service, Edgewood Arsenal. Bodansky,[2] while working with the Chemical Warfare Service, first noted the inhibiting power of di-isopropyl fluorophosphate on cholinesterase. When given intramuscularly, it is capable of lowering plasma and red-cell cholinesterase activity to a marked extent and for a prolonged period. The drug is also capable of improving muscle strength in patients with myasthenia gravis. It is not, however, a satisfactory drug to use from the clinical point of view. In the 7 patients treated by Comroe et al., 2 showed little or no benefit, 2 were considerably improved, 1 had marked beneficial effects, and in 2 the results were obscured by peculiarities in the natural cycle of the disease. In no case did the objective or subjective improvement following the administration of di-isopropyl fluorophosphate equal or exceed that produced by the use of neostigmine. Attempts, moreover, to give large doses of the drug resulted in nausea and vomiting and other symptoms referable to the central nervous system. Despite the fact that it lowered the plasma cholinesterase to zero, it produced less clinical improvement than neostigmine in patients with myasthenia gravis.

The reason for the relative failure of di-isopropyl fluorophosphate as a therapeutic agent has not been fully determined. Being a highly lipoid-soluble agent, whereas neostigmine is a highly water-soluble agent, it may not find its way into the myoneural junction as readily as does neostigmine. If the drug is given to man in doses large enough to produce improvement throughout the body, it cannot be administered regularly because of its untoward effects on the gastrointestinal tract and the nervous system. The better results obtained by neostigmine, however, may be due to the possibility that neostigmine has a direct action on skeletal muscles that is not shared by di-isopropyl fluorophosphate. Whatever final conclusions are reached regarding the reason for its relative failure, the drug may prove to be of some use when utilized, in nontoxic doses, to obtain its prolonged effect. At the same time neostigmine can be given to obtain the characteristically stronger action. Since neostigmine, however, tends to protect cholinesterase from inactivation by di-isopropyl fluorophosphate, it seems unlikely that the latter will ever be as valuable as neostigmine in the treatment of myasthenia gravis.

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MASSACHUSETTS MEDICAL SOCIETY

DEATH

SNOW — Henry C. B. Snow, M.D., of Buzzards Bay, died May 27. He was in his seventy-first year.

Dr. Snow received his degree from Tufts College Medical School in 1897. He was a former member of the Massachusetts Medical Society.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

NEW APPOINTMENTS

Victoria M. Cass, M.D., has been appointed epidemiologist in the Division of Administration, Massachusetts Department of Public Health. Dr. Cass held the position of teaching fellow in pathology at Tufts College Medical School from 1942 to 1944. Prior to her recent appointment, she was house officer, Medical Service, Boston City Hospital.

Joseph H. Hanson, M.D., formerly of the Medical Corps, A.U.S., has been appointed epidemiologist in the Division of Communicable Diseases, Massachusetts Department of Public Health.

Margaret M. Haehnel, M.S., has been appointed public-health social-work supervisor in the South Metropolitan District of the Massachusetts Department of Public Health. Mrs. Haehnel has been associated with the Worcester Children's Friend Society, the Family Welfare Society, of Springfield, and the Pondville Cancer Hospital.

Claire F. Ryder, M.D., formerly research resident and teaching fellow in tropical medicine at the Boston City Hospital, has been appointed epidemiologist in the Division of Administration, Massachusetts Department of Public Health. Prior to attending the Army Medical School in Washington, D. C., Dr. Ryder was house officer at the Boston City Hospital.

A. Geraldine White, A.B., has been appointed research consultant in the Child Growth and Development Program, Division of Maternal and Child Health, Massachusetts Department of Public Health. Miss White formerly held the position of health education assistant with the Middlesex Health Association.

Isah L. Salzman, M.S., who held the position of social worker with the Boston Department of Public Welfare, has been transferred to the Northeastern District of the Massachusetts Department of Public Health.

Brooks Ryder, M.D., a former captain in the Medical Corps, A.U.S., has been appointed epidemiologist in the Division of Local Health Administration, Massachusetts Department of Public Health. Prior to his appointment, Dr. Ryder was research assistant in anatomy at Tufts College Medical School. He served his internship at the Boston City Hospital.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Conduction Anesthesia. Clinical studies of George P. Pitkin, M.D. Edited by James L. Southworth, M.D., and Robert A. Hingson, M.D. 4°, cloth, 981 pp., with 606 illustrations. Philadelphia: J. B. Lippincott Company, 1946. $18.00.

Modern Management in Clinical Medicine. By F. Kenneth Albrecht, M.D., senior assistant surgeon, United States Public Health Service, and Kansas State Tuberculosis Consultant. 4°, cloth, 1238 pp., with 237 illustrations. Baltimore: Williams and Wilkins Company, 1946. $10.00.

Intracranial Complications of Ear, Nose and Throat Infections. By Hans Brunner, M.D., associate professor of otolaryngology, University of Illinois College of Medicine. 8°, cloth, 444 pp., with 95 illustrations. Chicago: Year Book Publishers, Incorporated, 1946. $6.75.

Anesthesia in General Practice. By Stuart C. Cullen, M.D., head of Division of Anesthesiology, Department of Surgery, State University of Iowa Hospitals, and associate professor of surgery (anesthesiology), State University of Iowa College of Medicine. 8°, cloth, 260 pp., with 36 illustrations and 4 tables. Chicago: Year Book Publishers, Incorporated, 1946. $3.50.

Treatment of Bronchial Asthma. By Vincent J. Derbes, M.D., instructor in medicine and in preventive medicine, Tulane University of Louisiana School of Medicine, assistant visiting physician, Charity Hospital of Louisiana, and director of the Department of Allergy, Ochsner Clinic; and Hugo T. Engelhardt, M.D., instructor in clinical medicine, Baylor University College of Medicine, Houston, Texas, adjunct in medicine, Jefferson Davis Hospital, Houston, and visiting physician, Charity Hospital, New Orleans. With chapters by a panel of contributors. 8°, cloth, 466 pp., with 61 illustrations. Philadelphia: J. B. Lippincott Company, 1946. $8.00.

Peptic Ulcer: Its diagnosis and treatment. By I. W. Held, M.D., attending physician, Beth Israel Hospital; and A. Allen Goldbloom, M.D., assistant clinical professor of medicine, New York Medical College and Flower and Fifth Avenue Hospitals, associate physician, Beth Israel and Metropolitan hospitals, and associate cardiologist, Beth Israel Hospital, New York City. 8°, cloth, 383 pp., with 110 illustrations. Springfield, Illinois: Charles C Thomas, 1946. $6.50.

Shock Treatment and Other Somatic Procedures in Psychiatry. By Lothar B. Kalinowsky, M.D., research associate in psychiatry, Columbia University, College of Physicians and Surgeons, and New York State Psychiatric Institute and Hospital, and assistant neurologist, Neurological Institute of New York; and Paul H. Hoch, M.D., assistant clinical psychiatrist, New York State Psychiatric Institute and Hospital, and instructor in psychiatry, Columbia University College of Physicians and Surgeons. With a foreword by Nolan D. C. Lewis, M.D., professor of psychiatry, Columbia University College of Physicians and Surgeons, and director, New York State Psychiatric Institute and Hospital. 8°, cloth, 294 pp. New York: Grune and Stratton, 1946. $4.50.

Clinical Methods of Neuro-ophthalmologic Examination. By Alfred Kestenbaum, M.D., assistant clinical professor of ophthalmology, New York University, lecturer in ophthalmology, Mt. Sinai Hospital, associate ophthalmologist, City Hospital, consultant ophthalmologist, Psychiatric Department, Bellevue Hospital, and Neurologic Department, Goldwater Memorial Hospital. 8°, cloth, 384 pp., New York: Grune and Stratton, 1946. $6.75.

Early Ambulation and Related Procedures in Surgical Management. By Daniel J. Leithauser, M.D., chief of surgery, St. Joseph Mercy Hospital, Detroit. 8°, cloth, 232 pp., with 36 illustrations and 6 tables. Springfield, Illinois: Charles C Thomas. 1946. $4.50.

Practical Malariology. Prepared under the auspices of the Division of Medical Sciences, National Research Council, by Paul F. Russell, M.D., M.P.H., Parasitology Division, Army Medical School, Luther S. West, Ph.D., head of Biology Department, Northern Michigan College of Education, and Reginald D. Manwell, Sc.D., professor of zoology, Syracuse University. 8°, cloth, 683 pp., with 238 illustrations. Philadelphia: W. B. Saunders Company, 1946. $8.00.

Carbohydrate Metabolism: Correlation of physiological, biochemical and clinical aspects. By Samuel Soskin, M.D., director of the Research Institute, Michael Reese Hospital, medical director, Michael Reese Hospital, and professorial lecturer in physiology, University of Chicago; and Rachmiel Levine, M.D., director of metabolic and endocrine research, Michael Reese Hospital. 8°, cloth, 315 pp., with 42 tables. Chicago: University of Chicago Press, 1946. $6.00.

The Traumatic Deformities and Disabilities of the Upper Extremity. By Arthur Steindler, M.D., professor and head, Department of Orthopedic Surgery, State University of Iowa College of Medicine. In collaboration with John L. Marxer, M.D., associate, Orthopedic Department, State University of Iowa College of Medicine. 4°, cloth, 494 pp., with 443 illustrations. Springfield, Illinois: Charles C Thomas, 1946. $10.00.

Operative Gynecology. By Richard W. Te Linde, M.D., professor of gynecology, Johns Hopkins University School of Medicine, and chief gynecologist, Johns Hopkins Hospital. 8°, cloth, 751 pp., with 309 illustrations and 9 color plates. Philadelphia: J. B. Lippincott Company, 1946. $18.00.

Diseases of the Basal Ganglia and Subthalamic Nuclei. By D. Denny-Brown, M.D., C.H.C., D.Ph., F.R.C.P., professor of neurology, Harvard Medical School, and director of Neurological Unit, Boston City Hospital. 8°, cloth, 74 pp., with one colored plate. New York: Oxford University Press, 1946. $2.50. Reprinted from *Oxford Loose-Leaf Medicine.*

The Diagnosis and Treatment of Bronchial Asthma. By Leslie W. Gay, Ph.D., M.D., assistant professor of medicine, Johns Hopkins University School of Medicine and director, Allergy Clinic, Johns Hopkins Hospital. With a foreword by Warfield R. Longcope, M.D., professor of medicine, Johns Hopkins University School of Medicine, and physician-in-chief, Johns Hopkins Hospital. 8°, cloth, 334 pp., with 80 illustrations, 5 plates and 39 tables. Baltimore: Williams and Wilkins Company, 1946. $5.00.

RKG Rheocardiography: A method of circulation's investigation and diagnosis of circular motion. By W. Holzer; K. Polzer; and A. Marko. From the Nerve Clinic, the Physiologic Institute and the Pharmacologic Institute of the University of Vienna. Translated by Mrs. Emma M. Kreidl. 8°, paper, 43 pp.; with 44 illustrations. Vienna: Wilhelm Mandrich, 1946.

The Differential Diagnosis of Jaundice. By Leon Schiff, Ph.D., M.D., associate professor of medicine, Department of Internal Medicine, University of Cincinnati College of Medicine, and director, Gastric Laboratory, Cincinnati General Hospital. 8°, cloth, 313 pp., with 38 illustrations. Chicago: Year Book Publishers, Incorporated, 1946. $5.50.

The Chest: A handbook of roentgen diagnosis. By Leo G. Rigler, M.D., professor and chief, Department of Radiology, University of Minnesota Medical School. 8°, cloth, 352 pp., with 338 illustrations. Chicago: Year Book Publishers, Incorporated, 1946. $6.50.

Their Mother's Sons. By Edward A. Strecker, M.D., Sc.D., Litt.D., LL.D. 8°, cloth, 220 pp. Philadelphia: J. B. Lippincott Company, 1946. $2.75.

A Manual of Tomography. By M. Weinbren, B.Sc., M.R.C.S. (Eng.), L.R.C.P. (Eng.), F.F.R. (Lond.), D.M.R.E. (Camb.), adviser in radiology, Union Defence Force, and radiologist, Chamber of Mines Hospital, Johannesburg. 4°, cloth, 270 pp., with 397 illustrations. London: H. K. Lewis and Co., Limited, 1946. Sh. 45.

Studies of Compulsive Drinkers. Part I: *Case histories.* By Herman Wortis, M.D.; and Leonard R. Sillman, M.D. Part II: *Psychological test results.* By Florence Halpern, M.A. Edited by Jane F. Cushman, M.A., and Carney Landis, Ph.D. With a foreword by Nolan D. C. Lewis, M.D. 8°, paper, 90 pp. New Haven: Hillhouse Press, 1946. $1.00.

Principles in Roentgen Study of the Chest. By William Snow, M.D., director of radiology, Bronx Hospital, and roentgenologist-in-charge, Harlem Hospital, New York City. 8°, cloth, 414 pp., with 508 illustrations. Springfield, Illinois: Charles C Thomas, 1946. $10.00.

Medical Research: A symposium. Edited by Austin Smith, M.D. 8°, cloth, 169 pp., with 17 illustrations. Philadelphia: J. B. Lippincott Company, 1946. $5.00.

Unhappy Marriage and Divorce: A study of neurotic choice of marriage partners. By Edmund Bergler, M.D. With an introduction by A. A. Brill, M.D. 8°, cloth, 167 pp. New York: International Universities Press, 1946. $2.50.

Acetanilid: A critical bibliographic review. By Martin Gross, M.D., research assistant and assistant professor, Laboratory of Applied Physiology, Yale University School of Medicine. With an introduction by Howard W. Haggard, M.D., director, Laboratory of Applied Physiology, Yale University School of Medicine. 8°, cloth, 155 pp., with 8 illustrations. New Haven: Hillhouse Press, 1946. $3.00.

Narcotics and Drug Addiction. By Erich Hesse, M.D. 8°, cloth, 219 pp. New York: Philosophical Library, 1946. $3.75.

The Biology of Schizophrenia. By R. G. Hoskins, Ph.D., M.D., director of research, Memorial Foundation for Neuro-Endocrine Research, Harvard Medical School, and Worcester State Hospital. 8°, cloth, 192 pp. New York: W. W. Norton and Company, Incorporated, 1946. $2.75.

Medical Education and the Changing Order. By Raymond B. Allen, M.D., Ph.D., executive dean, Colleges of Dentistry, Medicine and Pharmacy, University of Illinois. Chicago. Studies of the Committee on Medicine and the Changing Order, New York Academy of Medicine. 8°, cloth, 142 pp. New York: The Commonwealth Fund, 1946. $1.50.

Renal Diseases. By E. T. Bell, M.D., professor of pathology, University of Minnesota Medical School. 8°, cloth, 434 pp., with 115 illustrations. Philadelphia: Lea and Febiger, 1946. $7.00.

Allergy in Theory and Practice. By Robert A. Cooke, M.D., Sc.D., attending physician and director, Department of Allergy, Roosevelt Hospital, New York City. In association with Horace S. Baldwin and others. 8°, cloth, 572 pp., with a color plate. Philadelphia: W. B. Saunders Company, 1946. $8.00.

An Integrated Practice of Medicine. By Harold Thomas Hyman, M.D. Four volumes and index volume. 8°, cloth, 4131 pp., with 1184 illustrations, 305 in color, and 319 diagnostic tables. Philadelphia: W. B. Saunders Company, 1946. $50.00.

The Anatomy of the Bronchial Tree: With special reference to the surgery of lung abscess. By R. C. Brock, M.S. (Lond.), F.R.C.S. (Eng.), surgeon to Guy's Hospital, Brompton Hospital and E. M. S. Thoracic Surgical Centre. 8°, cloth, 96 pp., with 142 illustrations. New York: Oxford University Press, 1946. $12.00.

Gastroenterology in General Practice. By Louis Pelner, M.D., associate attending physician, Greenpoint Hospital, Brooklyn, associate visiting physician, Brooklyn Cancer Institute, and adjunct physician, Beth Moses Hospital, Brooklyn. With the collaboration of Louis A. Held, M.D., attending roentgenologist, Beth Moses Hospital, Brooklyn. With contributions from Alexander Lewitan, M.D., consulting roentgenologist, Norwegian Public Health Service, New York, and adjunct roentgenologist, Beth Israel Hospital, New York; Samuel Waldman, M.D., associate attending physician, Greenpoint Hospital, Brooklyn; and Siegfried W. Westing, M.D., roentgenologist, Brooklyn Cancer Institute. 8°, cloth, 285 pp., with 108 illustrations and 15 tables. Springfield, Illinois: Charles C Thomas, 1946. $7.50.

The Ego and the Mechanisms of Defense. By Anna Freud. Translated from the German by Cecil Baines. 12°, cloth, 196 pp., New York: International Universities Press, Incorporated, 1946. $4.00.

Chronic Diseases and Psychological Invalidism: A psychosomatic study. By Jurgen Ruesch, M.D. With a foreword by Karl M. Bowman, M.D. From the Division of Psychiatry, University of California Medical School, and Langley Porter Clinic, San Francisco. 8°, paper, 191 pp. New York: American Society for Research in Psychosomatic Problems, 1946. $3.00.

Urgent Surgery. Edited by Julius L. Spivack, M.D., associate professor of surgery, University of Illinois College of Medicine, senior attending surgeon, Columbus Memorial Hospital, Chicago, and attending surgeon, Oak Forest Infirmary. Volume I. 8°, cloth, 714 pp., with 244 illustrations. Springfield, Illinois: Charles C Thomas, 1946. $10.00.

Penicillin in Neurology. By A. Earl Walker, M.D., associate professor of neurologic surgery, University of Chicago School of Medicine; and Herbert C. Johnson, M.D., resident neurologic surgeon, University of Chicago School of Medicine. 8°, cloth, 202 pp., with 72 illustrations. Springfield, Illinois: Charles C Thomas, 1946. $5.00.

Psychiatric Interviews with Children. Edited by Helen Leland Witmer. 8°, cloth, 443 pp. New York: The Commonwealth Fund, 1946. $4.50.

Personality of the Preschool Child: The child's search for his self. By Werner Wolff, professor of psychology, Bard College. 8°, cloth, 341 pp., with 118 figures. New York: Grune and Stratton, 1946. $5.00.

Surgical Treatment of the Soft Tissues. Edited by Frederic W. Bancroft, M.D., associate clinical professor of surgery, Columbia University, attending surgeon, New York City and Beth David hospitals, consulting surgeon, Veterans Administration, Lincoln and Harlem hospitals, New York City, and Kings Park State Hospital, Kings Park, New York; and George H. Humphreys, II, M.D., Sc.D., Valentine Mott Professor of Surgery, Columbia University College of Physicians and Surgeons, and director of Surgical Service, Presbyterian Hospital, New York City. 4°, cloth, 520 pp., with 244 illustrations. Philadelphia: J. B. Lippincott Company, 1946. $15.00.

Adjustment to Physical Handicaps and Illness: A survey of the social psychology of physique and disability. By Roger G. Barker, Beatrice A. Wright and Mollie R. Gonick. 8°, paper, 372 pp. New York: Social Science Research Council, 1946. $2.00.

Radical Surgery in Advanced Abdominal Cancer. By Alexander Brunschwig, M.D., professor of surgery, University of Chicago. 8°, cloth, 324 pp., with 117 illustrations and 16 tables. Chicago: University of Chicago Press, 1947. $7.50.

Textbook for Psychiatric Attendants. By Laura W. Fitzsimmons, R.N., B.S., M.A., assistant director of nurses and chief neuropsychiatric nurse, United States Veterans Administration, and chairman, Committee on Psychiatric Nursing, National League of Psychiatric Nursing. 8°, cloth, 332 pp. New York: Macmillan Company, 1946. $3.50.

Diagnosis and Treatment of Menstrual Disorders and Sterility. By Charles Mazer, M.D., assistant professor of gynecology and obstetrics, Graduate School of Medicine, University of Pennsylvania, and gynecologist, Mount Sinai Hospital, Philadelphia; and S. Leon Israel, M.D., instructor in gynecology and obstetrics, University of Pennsylvania School of Medicine, and associate gynecologist, Mount Sinai Hospital, Philadelphia. Second edition revised and enlarged. 8°, cloth, 570 pp., with 133 illustrations. New York: Paul B. Hoeber, Incorporated 1946. $7.50.

Radiology for Medical Students. By Fred J. Hodges, M.D., professor and chairman, Department of Roentgenology, University of Michigan Medical School; Isadore Lampe, M.D., associate professor, Department of Roentgenology, University of Michigan Medical School; and John F. Holt, M.D., assistant professor, Department of Roentgenology, University of Michigan Medical School. 8°, cloth, 424 pp., with 103 plates. Chicago: Year Book Publishers, Incorporated, 1947. $6.75.

Adolescent Sterility: A study in the comparative physiology of the infecundity of the adolescent organism in mammals and man. By M. F. Ashley Montague, associate professor of anatomy, Hahnemann Medical College and Hospital, Philadelphia, and visiting lecturer, Department of Sociology, Harvard University. 8°, cloth, 148 pp., with 33 tables. Springfield, Illinois: Charles C Thomas, 1946. $3.50.

Penicillin in Syphilis. By Joseph E. Moore, M.D., associate professor of medicine and adjunct professor of public-health administration, Johns Hopkins University School of Medicine, physician-in-charge, Syphilis Division of the Medical Clinic, and visiting physician, Johns Hopkins Hospital, chairman, Syphilis Study Section, National Institute of Health, United States Public Health Service, and chairman, Subcommittee on Venereal Diseases, National Research Council. 8°, cloth, 319 pp., with 57 illustrations and 52 tables. Springfield, Illinois: Charles C Thomas, 1946. $5.00.

Military Neuropsychiatry. Proceedings of the Association for Research in Nervous and Mental Diseases. Volume XXV. 8°, cloth, 366 pp. Baltimore: Williams and Wilkins Company, 1946. $6.00.

Postgraduate Obstetrics. By William F. Mengert, professor and chairman, Department of Obstetrics and Gynecology, Southwestern Medical College, and chairman, Obstetrics and Gynecology, Parkland Hospital, Dallas, Texas. 8°, cloth, 392 pp., with 123 illustrations. New York: Paul B. Hoeber, Incorporated, 1946. $5.00.

Uterine Contractibility in Pregnancy: A study of the contractions of pregnancy and labor under normal and experimental conditions. By Douglas P. Murphy, M.D., assistant professor of obstetrics and gynecology and research associate in the Gynecean Hospital Institute of Gynecologic Research, University of Pennsylvania School of Medicine. 4°, cloth, 134 pp., with 64 illustrations. Philadelphia: J. B. Lippincott Company, 1946. $5.00.

NOTICES

RESIDENCY IN RADIOLOGY

Applications will be considered for appointment to a residency in radiology at the Joseph H. Pratt Diagnostic Hospital and Boston Dispensary from physicians with one or two years of training in radiology. There are about 1800 diagnostic cases monthly, as well as a tumor clinic and therapy and teaching conferences. Appointments will be made for one year beginning September 1, 1947.

Applications should be addressed to Mr. Richard T. Viguers, administrator, Joseph H. Pratt Diagnostic Hospital, 30 Bennet Street, Boston 11.

SOUTH END MEDICAL CLUB

The next regular meeting of the South End Medical Club will be held at the Prendergast Preventorium, 1000 Harvard Street, Mattapan, on Tuesday, June 24, at twelve noon. Dr. Eli Friedman will speak on the subject "Some Interesting Problems in Pediatrics."

This meeting will mark the twentieth anniversary of the Club.

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